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Public Health

LAMONT, D. Joan & MACQUEEN, I. A. G. **One Approach to Health Education.** *Med. Officer.* 1958, Oct. 31, v. 100, No. 18, 279–84, 1 diagram.

"The National Health Service costs £700 million a year, three-fifths of the money being spent on hospital treatment of disease; sickness benefit costs another £100 million; and 200,000,000 working days are lost each year through illness." These losses must continue until the incidence of sickness is reduced by preventive measures and in the opinion of the authors of this paper "The main available method of prevention is health education".

The approaches and techniques in individual and group health teaching must be adapted to changing needs and demands of the people. Health education with particular reference to the experience of the authors in Aberdeen is described and discussed at some length. In group education, school medical officers, school health visitors and school teachers must of course continue to inculcate personal hygiene to elementary schoolchildren, but in addition there are special groups which require teachers and these are: (1) prospective parents, (2) parents of young children, (3) adolescents and older children and (4) the "Elders of the Tribe". Individual teaching is next described with discussion of some of its difficulties. For group teaching at least "five brands of health education officer have evolved" which are: (1) medical officers for health education, (2) school teachers (preferably with degrees in biology and some training in health), (3) specialist health visitors, (4) health visitor tutors and (5) tutors from general or mental hospitals.

The Aberdeen scheme of health education is next described and discussed under the headings of personnel, the preparation for group teaching, the courses for prospective parents, parents' clubs and teaching methods —didactic teaching, demonstration, group discussion and visual aids. The visual aids employed are posters, blackboard, flannelgraph, filmstrips and slides, epivisor, films and "hand-outs".

"We think that our audiences have learned a little and that the Health Department has gained new status in their eyes; and, since teaching is a two-way traffic, we have learned too." *M. E. Delafield*

ROBERTS, Llywelyn [M.D., M.R.C.P., D.P.H.] assisted by Kathleen M. SHAW, M.B.E. **A Synopsis of Hygiene** (JAMESON and PARKINSON). 11th Edition. pp. viii + 694, 22 illustrations. 1958. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [60s.]

[This book was reviewed on p. 103.]

Maternal and Child Health

TOWNSEND, L. **Radiation Hazards to the Foetus.** *Med. J. Australia.* 1958, Aug. 30, v. 2, No. 9, 289–90.

An inquiry has been begun into the immediate and remote obstetrical consequences of every pelvimetry in pregnancy made at the Royal Women's Hospital, Melbourne, since 1946. Meanwhile a study has been made of the previous history of 204 children under 10 years of age who have died from leukaemia in the past decade. The parents of 171 of them were traced by letter and questionnaire and only 12 mothers (7%) had had an X-ray examination during pregnancy (10 of the abdomen and 2 pelvimetry). In other words, in Victoria, of some 20 child deaths yearly from leukaemia there was only about 1 per annum whose mother had had an X-ray examination during pregnancy.

[The lack of information from 16% of the parents is a serious drawback which might affect the results of this small scale inquiry.] *A. Bradford Hill*

HOWORTH, Irene E. **Screening Tests of Hearing in Pre-School Children, with particular reference to Selective Testing.** *Med. Officer.* 1958, Nov. 14, v. 100, No. 20, 307–8.

This is a report on the results of screening tests of pre-school children carried out by health visitors who had been specially trained for this purpose. This was part of a scheme agreed upon by the Lancashire County Council for the ascertainment of deafness in young children and the training of young deaf children as part of the welfare provisions under the National Health Service Act, 1946. Included in the scheme was the setting up of a clinic for determining the diagnosis of deafness in those children who had failed in the screening tests. From the early experience of screening it appeared desirable to discover the children who were at special risk of deafness and to concentrate on the testing of these. A list of 9 categories of children "at risk" or belonging to these vulnerable groups was drawn up and is given in the paper. The findings of the screening tests and the diagnostic clinic are described and set out in tables. Among the findings were that of 5,531 of the children in the general population 31 (5·6 per 1,000) failed in 3 screening tests and of these 31 children 14 (2·53 per 1,000 children tested) were diagnosed as deaf. In comparison, in the testing at a later period of 662 children in the vulnerable groups 10 (15·1 per 1,000 children) failed in the screening tests and of these 10 children 6 (9·06 per 1,000 children tested) were diagnosed as deaf.

M. E. Delafield

ARCHER, Nora E. R. **Word Tests as a Method of Screening for Deafness in School Children.** *Med. Officer.* 1958, Nov. 14, v. 100, No. 20, 308–11.

In this paper the author describes the word and sentence tests of hearing which she has used since 1956 in periodic school medical inspection. Over 3,000 children have been tested and in addition the method has been used at re-examinations, special examinations and examinations for the ascertainment of physical and mental handicap. It has also come to be used with younger children at child welfare clinics and with adults at examination for appointments and college entrance. There is a general account of the tests and their complication with sections on the method of approach to the children who are to be tested and the errors which might result from the various noises which exist at different times in the school or its surroundings. Some of the results of testing are recorded. There is a good discussion in which it is also stated "Free field testing with a variable and uncalibrated source of sound under variable acoustic conditions cannot be expected to measure accurately individual hearing acuity. The basic necessity, however, is not an accurate assessment of each child's hearing, . . . but to screen numbers of children with average hearing for the occasional child with hearing seriously below average".

M. E. Delafield

GREENBERG, M., JACOBZINER, H., MCLAUGHLIN, Mary C., FUERST, H. T. & PELLITTERI, O. **A Study of Pica in relation to Lead Poisoning.** *Pediatrics.* Springfield, Ill. 1958, Oct., v. 22, No. 4, Pt. 1, 756–60, 1 fig. [15 refs.]

"Only in comparatively recent years has attention been called" to the toxic effect of lead on children, in whom the diagnosis can easily be overlooked. In most states this lead poisoning is not reportable, but in New York City the condition is notifiable and in the years 1950–7 the total of notifications was 416. Reasons are given for believing that the actual number of cases is higher than this. Many investigators point to the close association of lead poisoning in children with the habit of pica [this *Bulletin*, 1956, v. 31, 690]. The study described in this paper had as its object the estimation of the extent of this association. The method of study was to ask parents at the child health stations of New York City, where about 160,000 infants and young children attend annually, whether any of the family had manifestations of pica. If so a specimen of blood was taken and analysed for lead, and the public health nurse made follow-up visits to the family. A diagnosis of lead poisoning was considered to be established if the concentration of lead in the blood was 0·06 mgm. per 100 ml. or more and 2 or more of the following symptoms or signs were present: (1) gastro-intestinal symptoms, (2) neurological symptoms, (3) anaemia, marked pallor, basophilic stippling of blood cells or blue gum line, and (4) X-ray evidence of increased density at the metaphyses of the long bones. The results of the study during 1956 and 1957 are described with tables and figures. A total of 194 children with pica was found and among this number there were 28 (14%) cases of lead poisoning and 20 (10%) probable cases of lead poisoning. The cases were chiefly in children aged 1, 2 and 3 years and were about equally divided between boys and girls. It is of interest that no lead poisoning was found in the 24 (12%) children who were under 1 year of age, probably because the paint for cribs and toys is now either lead free or contains less than 1% of lead.

M. E. Delafield

Vital Statistics and Epidemiology

DE ALMEIDA, A. S. & RODRIGUES, R. C. Mortalidade infantil em 19 Municípios do Estado de Pernambuco (1951–1955). [**Infant Mortality in 19 Municipal Areas in the State of Pernabuco, Brazil, in 1951–1955**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1957, Dec., v. 9, No. 2, 107–31, 5 graphs. English summary (9 lines).

Infant mortality has been studied in 5 geographical groups comprising 19 municipal areas. The deaths are available from civil registration but the records of live births are so defective that the numbers must be estimated (as upper and lower limits by applying to the total population birth rates of 45 and 55 per 1,000). Even the lower figures derived from these estimates show infant mortality rates in the 5 groups of 173, 242, 245, 278 and 334 per 1,000 per annum. Of the total 66,178 deaths recorded at all ages 37,385 (56·5%) occurred in the first year of life. In 2 specific municipal areas the infant mortality rate was over 400 per 1,000 in the period 1951–5 and in one-third of them the infant deaths comprised over 60% of the total mortality. Of the total infant deaths only 27% took place in the first month of life and the remaining 73% at 1–11 months. In the years 1951–5 there was no improvement in these excessively high rates of infant loss. *A. Bradford Hill*

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order:—General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.

BANKS, H. S. **Infection across the Intact Conjunctiva.** *Lancet.* 1958, Sept. 6, 518–19.

In this annotation Banks brings together the evidence collected by Karola PAPP [this *Bulletin*, 1955, v. 30, 941; 1956, v. 31, 985] that measles is transmitted from child to child across the conjunctival mucous membrane, and that infection can be prevented if a drop of convalescent serum is instilled into each eye of a normal child within a few hours after exposure to infection. He links these findings with those of MOORE [*ibid.*, 1958, v. 33, 163] who showed that infection of guinea-pigs with *Salmonella enteritidis* may be prevented by protecting their eyes with goggles before exposing them to the infection.

[The annotation forms a striking argument for a new conception of transmission, which may have important implications.] *Charles Wilcocks*

WEBSTER, C. U. **Staphylococcal Diarrhoea.** *Lancet.* 1958, Nov. 15, 1036–8. [10 refs.]

Much has been heard of epidemics of post-operative staphylococcal enteritis in surgical wards, associated with invasion of the bowel by antibiotic-resistant staphylococci. This series of 8 cases, with 5 deaths, appeared *sporadically* in 6 different surgical units in a hospital over a period of 4 months. This is disturbing since there is no reason to suppose that it is exceptional, and since the diagnosis may not be obvious clinically, nor even at necropsy, bacteriological examination is essential.

The condition is characterized by a grossly abnormal faecal flora, with enormous numbers of staphylococci and pus cells, and the virtual absence of Gram-negative bacilli and other organisms on direct film. In the 6 severe cases there were high temperatures, but in the 2 moderate cases there was little constitutional upset. After operation a sharp rise in temperature, a tympanitic abdomen, a temporary increase in bowel sounds, and diarrhoea, form a tetrad of clinical signs which should strongly suggest staphylococcal diarrhoea. The mucosal lesion leads to failure of resorption of alimentary secretions, to large losses of extracellular fluid, and so to hypotension. 1 patient, after initial resuscitation from shock, required 1 litre of glucose saline per hour for 8 hours before the circulation became stable.

The antibiotic in current use should be discontinued.

In most cases the staphylococci isolated are resistant to all the common antibiotics, but if erythromycin has been used only for contingencies, as in this hospital, they are usually erythromycin-sensitive. If they are not, the next choice of drug is novobiocin.

H. Stanley Banks

BURNETT, W., MCDONALD, Sheila & TIMBURY, Morag C. **Post-Operative Wound Infection. An Investigation into the Sepsis Rate in a General Surgical Unit.** *Scottish Med. J.* Glasgow. 1958, Sept., v. 3, No. 9, 392–7, 1 fig. [14 refs.]

Of 273 operations carried out in one surgical unit in Glasgow in a 7-month period from December 1956 (including all operations except haemorrhoidectomy and incision of primary abscesses), 211 were considered clean and 62 contaminated at the time of operation. 12·3% of the clean wounds subsequently yielded pathogenic bacteria and 7·6% were clinically septic. For the contaminated wounds the rates were 24·2 and 16·1%. *Staphylococcus aureus* was by far the commonest pathogen, being isolated from 11 of the 16 septic wounds. 6 of the strains of staphylococci were of 1 type (52A/79), 5 having been operation infections due to a surgeon with a septic lesion [MCDONALD & TIMBURY, this *Bulletin*, 1958, v. 33, 172]. 3 of the infections were thought to be autogenous.

R. E. O. Williams

VERDE, B. Diagnostica clinica e di laboratorio delle principali virosi umane. [**Clinical and Laboratory Diagnosis of the Principal Virus Diseases of Man**] *Acta Med. Italica.* 1956, v. 11, 1–186, 45 figs. [Refs. in footnotes.]

In this long, illustrated monograph the author sums up, with many references to the literature, the clinical and laboratory diagnosis of the chief virus diseases of man. He divides the work into the following sections:—

Septicaemic diseases—yellow fever, dengue, sandfly fever.

Exanthematic diseases—smallpox, chickenpox, measles, rubella.

Herpetic diseases—herpes, herpes zoster.

Diseases of the nervous system—epidemic encephalitis (von Economo), seasonal encephalitis (Japanese, St. Louis, WEE, EEE etc.), rabies, poliomyelitis (including Coxsackie), lymphocytic choriomeningitis.

Diseases of the respiratory system—influenza, psittacosis-ornithosis, primary atypical pneumonia.

Diseases of other systems—lymphogranuloma venereum, cat-scratch disease, infectious mononucleosis, mumps, hepatitis, trachoma.

The monograph should prove most useful for readers of the Italian language. *Charles Wilcocks*

OBERMAN, J. W., GREGORY, K. O., BURKE, F. G., ROSS, S. & RICE, E. C. **Electrophoretic Analysis of Serum Proteins in Infants and Children. II. Serum Gamma-Globulin Levels in Selected Infections and "Hypersensitivity" Diseases in Childhood.** *New England J. of Med.* 1958, Oct. 30, v. 259, No. 18, 855–62. [12 refs.]

TASMAN, A., MINKENHOF, J. E., VINK, H. H., BRANDWIJK, A. C. & SMITH, L. **On the Pathogenesis of Diphtheria. V. Importance of Intravenous Injection of Diphtheria Serum.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1958, v. 24, No. 2, 161–86, 8 figs. [13 refs.]

This paper includes a number of observations on the excretion of antitoxin into the saliva after administration by the intramuscular and intravenous routes respectively. These show that a significant concentration of antitoxin is obtained within 1 hour after injection by the latter route but not by the former. The relative serum concentrations of antitoxin consequent on intramuscular and intravenous injection of patients are also presented, showing that the maximum concentration of antitoxin in the blood is attained much more rapidly by the intravenous route.

Finally, an extensive investigation is made of the relative values of intravenous and intramuscular serum administration in the control of experimental diphtheria in the guineapig. The superiority of the intravenous route was indicated by a smaller number of deaths, a lesser loss of weight in surviving animals, and a lesser incidence of paralysis and of cardiac lesions.

[The superiority of the intravenous administration of serum in large doses had, of course, been investigated in Denmark many years before and most of the findings could have been taken for granted from earlier work.]

A particularly useful feature of this communication is a very definite recommendation of the method to be adopted to eliminate all danger from intravenous injection of serum. It is recommended that a preliminary skin test should be made with 0·2 ml. of a 1 in 10 dilution of the serum. It is imperative that this should be injected intradermally so that a weal is produced. It is maintained that if no redness or swelling appears within an hour of this procedure the intravenous injection of the serum can safely be performed.

In the authors' experience, with "enzymatically purified, radically despeciated horse serum" no serious reactions had appeared in the many hundreds of patients injected, with the above precautions.

[For references to the previous 4 parts of this study, see this *Bulletin*, 1955, v. 30, 357, 1015.]

J. W. McLeod

FERRARONI, L. La bonifica dei portatori di bb. difterici con metodi diversi di trattamento. [**Amelioration of Diphtheria Carriers by Different Forms of Treatment**] *Riv. Italiana d'Igiene.* 1958, May–June, v. 18, Nos. 5/6, 209–18. English summary.

The results of the administration of 7 single and 2 combined preparations, which are described for the most part under trade names but appear to be antibiotics, to diphtheria carriers are given.

The total number of carriers investigated was 650 and the preparations which gave a favourable result and were tried on a considerable group of individuals were Hostangina [a preparation containing antitoxin, tricresol, camphor and other ingredients, made by

Sclavo, Siena] and Iloticina [presumably Ilotycin (erythromycin)].

[As very little is recorded about the bacterial criteria of cure, it is difficult to assess the value of this work.]

J. W. McLeod

JOHNSON, R. E. & HALL, A. P. **Rubella Arthritis Report of Cases studied by Latex Tests.** *New England J. of Med.* 1958, Apr. 10, v. 258, No. 15, 743–5. [16 refs.]

The authors describe the occurrence of arthritis in 10 female patients suffering from rubella. The arthritis involved the small and medium joints, and began in the fingers soon after the appearance of the rash and lasted about a week. [This is a well known complication of rubella.] Latex fixation tests, a variation of the sheep-cell agglutination test for rheumatoid arthritis, were unexpectedly found to be positive in 9 out of 10 patients with arthritis but in only 2 out of 7 non-arthritic cases. The authors speculate on the significance of this finding. *A. B. Christie*

ANDERSSEN, N. Letal parotitt. [**Fatal Cases of Mumps with Orchitis**] *Nordisk Med.* 1958, Nov. 27, v. 60, No. 48, 1717–18, 1 fig.

The English summary appended to the paper is as follows:—

"A case of mumps with orchitis, which ended fatally, is reported. The patient was treated with cortisone, corticotropin and antibiotics. He had severe headache, confusion of mind, and the tendon reflexes were absent, whereas the spinal fluid was normal. Necropsy revealed multiple perivascular hemorrhages in the white matter of the brain and brain stem, but no signs of glial proliferation or demyelination were seen."

RITTER, B. S. **Mumps Meningoencephalitis in Children.** *J. Pediatrics.* St. Louis. 1958, Apr., v. 52, No. 4, 424–33, 1 fig. [27 refs.]

In this paper the author summarizes his experience of mumps meningo-encephalitis occurring in children under 14 years of age. The number of patients suffering from this illness was 30, the average age being 7·4 years and males constituting 19 of the total. Cases occurred at all seasons but were most prevalent in the spring and summer, and the interesting point emerged that meningo-encephalitis with parotitis was most frequent in the spring and meningo-encephalitis without parotitis was most frequent in the summer. Those in the latter group numbered 13, the diagnosis being made by serological methods. In the 17 associated with parotitis the salivary gland swelling appeared at intervals ranging from 9 days before to 5 days after the meningo-encephalitis. Sublingual, submaxillary or testicular involvement were absent in all 30 patients. Abdominal pain was a persistent and severe feature in 4 instances and after serum amylase determinations 3 patients were considered to have mumps pancreatitis. The degree of illness was assessed as negligible in 2, mild in 7, moderate in 17 and severe in 4, 2 of the last mentioned suffering from generalized convulsions.

Treatment was principally symptomatic and supportive, adreno-corticotrophic hormone given to 2 children producing no measurable effect on the course of the disease. Sequelae appeared in the shape of staring spells in a 6-year-old boy 2 years after convalescence. Serological evidence of mumps infection requires the demonstration of significant differences in antibody titres in paired sera, one drawn early and the other late in the disease. However, this author claims that in 60% of cases of subsequently proved mumps meningo-encephalitis a presumptive diagnosis of mumps infection can be made from the antibody titres of the first serum sample, provided the anti-S antibody titre is significantly higher than the anti-V antibody. *A. Joe*

MÖBEST, H. Über Antikörperbildung bei Mumps nach Scharlach. [**Antibody Formation in Mumps developing after Scarlet Fever**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 171, Nos. 6/7, 425–9.

Serological examinations have been carried out on a child aged 6 years who developed mumps 11 days after admission to hospital suffering from scarlet fever, which responded normally to penicillin treatment. The development of V and S mumps complement-fixing antibodies was delayed, and they were first detected 21 days after the appearance of parotitis, when an anti-V titre of 32 and an anti-S titre of 16 were recorded. After 84 days the titres had fallen to 8. A similar case was observed in a child aged 5 years, who was admitted to hospital suffering from scarlet fever and placed in the same ward as the first child. He was treated with 2 cc. of gamma-globulin as a prophylaxis against mumps infection, but in spite of this he developed mumps after returning home, 19 days after the onset of parotitis in the first patient and 27 days after developing scarlet fever. The V and S antibody titres of the gamma-globulin were both 8. In the patient's serum the titres were 64 and 16 on the 33rd day after the appearance of parotitis and 64 and 32 on the 64th day. *D. J. Bauer*

FELKAI, D. **Evaluation of a New Type of Mumps Vaccine in Humans.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 2, 193–6. [15 refs.]

An investigation has been made of the efficacy of a mumps vaccine prepared from the Enders strain of mumps virus adsorbed on to aluminium hydroxide and inactivated with formaldehyde. The finished product contained 5×10^4 haemagglutinating doses and 0·8 mgm. of gel per cc. 91 persons who gave negative results in skin tests with mumps virus antigen were given 2 intramuscular injections of 0·5 cc. of vaccine with an interval of 6 weeks; 3 months after the first injection 79·2% had developed a positive reaction, and the percentage of positive results in haemagglutination-inhibition tests had risen from 20·4 to 97·8, and in complement-fixation tests with V antigen from 0 to 96·7 and with S antigen from 5·2 to 77·3. A similar degree of immunity was also observed in 13 persons 3 months after the injection of a single dose of vaccine. *D. J. Bauer*

PETRILLA, A. & BARSY, G. **Vaccination against Pertussis. An Appraisal of its Efficacy.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 1, 35–42, 5 figs. [20 refs.]

The authors have attempted to assess the effectiveness of immunization against *Haemophilus pertussis* by analysing the morbidity figures for whooping cough since 1953 in Hungary, where immunization is compulsory. It was found that immunization had been effective in 20%–30% of children 1–3 years old, who had only 1 course of inoculations and 50% effective in children 2 years old, who had received 2 courses of inoculations. It is concluded that to reduce significantly the morbidity rate of pertussis, immunization must begin in early infancy.

[Comparing these figures with the results reported by the Medical Research Council's Whooping Cough Immunization Committee (see, for example, this *Bulletin*, 1957, v. 32, 228) it seems that the vaccine and schedule of inoculations used by the Hungarians are not giving the immunity that it is possible to achieve. The vaccine used, which is a combined diphtheria-pertussis-tetanus antigen vaccine, containing alum, has as its pertussis component an extract of pertussis organisms. *H. pertussis* organisms which are grown on a solidified semi-synthetic medium are suspended in saline, frozen and thawed 9 times and centrifuged. The supernatant, which is treated with formalin, is combined with the diphtheria and tetanus components to form the vaccine without any evidence being given of the potency of such an extract. It is accepted that 3 doses of pertussis vaccine are necessary for protection, but the Hungarians use only 2 doses which may also contribute to their failure to achieve a higher decrease in their morbidity rate for pertussis.] *F. T. Perkins*

POZSGI, N., SOARE, Irina, FAUR, Yvonne & TIGOIU, Viorica. Rezultatele vaccinărilor cu vaccin antipertusis preventiv în țară. [**The Results of Preventive Anti-*pertussis* Vaccinations in Rumania**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 151–61.

An account is given of the results of anti-pertussis vaccination carried out in Rumania between 1951 and 1956. The vaccine was inactivated with formaldehyde at room temperature, and contained 10,000 million *Haemophilus pertussis* per cc.; it was given in 3 doses of 2, 3 and 3 cc. respectively with intervals of 4 weeks. In 1951 6,000 doses were issued; the vaccine was well tolerated and in a group of 972 vaccinated children the subsequent incidence of pertussis was 1·8%, compared with 14–31% in unvaccinated groups. In 1953 8,000 doses were issued, and incidences of 0·9% and 4·4% were observed 6 months after vaccination in 525 vaccinated and 669 unvaccinated children respectively. On the basis of these and other results it was officially decided in 1955 to proceed to mass vaccination, using a total dose of 50,000 million organisms, and 26,000 doses of vaccine were prepared. The results were satisfactory, but are not presented in detail.

D. J. Bauer

LUPAȘCU, G. E. & OLARIU, T. Chimioprofilaxia tusei convulsive în unități închise de copii. [**Chemoprophylaxis of Whooping-Cough in Closed Communities of Children**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 163–9. [11 refs.] English summary.

An investigation has been made of the prophylactic effect of chloramphenicol against pertussis in children aged 3 months to 3 years living in 8 closed institutional communities. 49 children living in 4 communities who had been in contact with the infection 7–14 days previously were given chloramphenicol in a dose of 0·1 gm. per kgm. body weight, followed by one-half of this dose on the following day; 17 subsequently developed pertussis and the remaining 32 (65·3%) were apparently protected. In 2 other communities 31 children who had been exposed to infection 7–8 days previously were given chloramphenicol in a dose of 0·1 gm. per kgm. body weight on 2 successive days; 6 developed pertussis and 25 (80·5%) were protected. The remaining 2 communities were involved in a fully developed epidemic of pertussis; 24 children who had not yet developed the disease were given an initial dose of 0·1 gm. per kgm., followed by one-half of this dose on the 4 succeeding days, and 13 failed to develop the disease. *D. J. Bauer*

PROC. ROY. SOC. MED. 1958, June, v. 51, No. 6, 447–54 (United Serv. Sect. 21–8), 2 figs. **Discussion on Influenza** [HART, R. J. C.; BULOW, G. H.; JOHNSTONE, R. M.; PACE, T. A.]

This discussion by the United Services Section of the Royal Society of Medicine, London, covers the virological, clinical and epidemiological approach by the army authorities to the influenza epidemic of 1957. Virological studies demonstrated the occurrence of virus B influenza in the early part of the year with virus A (Asian 1957) taking over in the Far East at the end of April and invading Mediterranean and Home Commands from July onwards. Details are given of the technique of taking and transporting material and of the laboratory methods of investigation. A report of an outbreak in a small unit in Windsor follows with some detail of clinical features. An account of complications is given, the main one being staphylococcal pneumonia. The discussion ends with a description of the epidemic in Western Command. *A. B. Christie*

OWEN, I., PARKES, A. W., BULLOCK, J. & THORBURN, W. B. **Asian Influenza in a Royal Air Force Boy Entrants School.** *Pub. Health.* 1958, July, v. 72, No. 4, 134–42, 3 figs.

This paper describes 2 outbreaks of influenza due to the same virus in the same community during the autumn of 1957. The first and major outbreak was in September, when over a period of 19 days 899 cases occurred in a population of 1,827 boys and adults. During 26 days in late October and early November there were 110 cases, this being referred to by the authors as the minor outbreak. The boys were aged 15–17½ years and were organized in an initial training

squadron and 2 wings, the boys from each wing not mingling freely except at recreation and those in the training squadron hardly at all with the seniors. The adults mostly live apart from the boys and about one-third have little contact with them.

The major outbreak began in the beginning of September in one of the wings a few days after the return from holidays. 2 peaks of prevalence occurred, one on September 4 and the other on September 8 and 9. By September 10 there had been 680 cases but thereafter the epidemic rapidly declined, being virtually over by September 13. The cases among the boys totalled 799 with an incidence of 68%. Cases among adults reached a maximum on September 13, eventually totalling 100 with an incidence of 15%. The minor outbreak lasted from October 14 to November 8 and consisted of 94 cases among 1,500 boy entrants and 16 among 650 adult staff. On October 14 392 new boys had arrived from their homes in all parts of the country and 82 of the cases occurred among them.

The clinical features in both outbreaks were similar, but the authors draw attention to the fact that in the first malar flush and conjunctivitis were characteristic, whereas in the second infection of the throat was more common. There were no deaths and the complications consisted of 6 cases of pneumonia, 2 staphylococcal, in the first outbreak and 2 cases of pneumonia and 2 of otitis media in the second. Virological studies showed that the virus was the prevalent Asian type in both. Accommodation for the patients was a problem and was met by the utilization of hospital beds, those in the depleted dormitories and emergency beds in empty huts.

The main characteristics of the major outbreak were its explosiveness and the high attack rate. The minor outbreak started as soon as new boys arrived but no explosion occurred, and it is described as smouldering on with an attack rate low in comparison with the first outbreak. The low attack rate in the second outbreak was ascribed to an improved individual immunity possibly due to exposure to the influenza prevalent in the country as a whole. *A. Joe*

WOODALL, J., ROWSON, K. E. K. & MCDONALD, J. C. **Age and Asian Influenza, 1957.** *Brit. Med. J.* 1958, Nov. 29, 1316–18, 2 figs.

This is a study of the incidence of Asian influenza, with special reference to the effect of age, in a practice population of 1,732 patients on the outskirts of London during the autumn of 1957. A total of 31% of patients were affected—about one-half of the schoolchildren, one-third of the pre-school children, one-quarter of adults to age 60 and about one-eighth of older patients. Three-quarters of all patients affected were schoolchildren. The incidence of secondary cases was studied in 104 families; in 59 the disease was confirmed serologically. Secondary attack rates for all age-groups up to 40 varied little but fell away above that age. It seemed that the lower incidence in the older group was due not to lower susceptibility but to less exposure. Clinically the disease varied with age; drowsiness, vomiting, diarrhoea and nose bleeds were commoner in the youngest children, delirium in schoolchildren, while adults had headache, aches and pains, faintness and giddiness. *A. B. Christie*

HARBOE, A. Forløpet i Norge av influensapandemien forårsaket av virus av typen A/Asia/57. **[The Course in Norway of the Influenza Pandemic caused by Virus of the Type A/Asia/57]** *Nordisk Med.* 1958, Nov. 27, v. 60, No. 48, 1701–4, 4 figs.

The English summary appended to the paper is as follows:—

"Virus of the Asian type was first met with at Rjukan, a small inland town, where it started an epidemic at the end of August, 1957. Most of the country was struck by a major wave in the first half of October. In Oslo a second wave followed at Christmas Some remote areas in the upper North were not hit until December.

"School children and personnel living in military camps presented a particularly high morbidity. In a camp of 223 military recruits 88 per cent developed antibodies to the Asian type virus. Among the adult general population in Oslo the incidence of influenza (involving sick leave) was probably between 10 and 15 per cent. Twenty positive virus specimens were received from all parts of Norway; even as far north as Kjøllefjord at a latitude of 71°, in all of which strains of the Asian type were isolated, all but one at the influenza laboratory at the State Institute for Public Health in Oslo, which also carried out the typing. No other strains were found. They were submitted to the World Influenza Centre in London, where it was confirmed that they were characteristic Asian strains."

HELLER, L., KÖRLOF, B., MÖRNER, J. & ZETTERBERG, B. Influensaepidemien i Sverige 1957–1958. Vaccinationsförsök. **[The Influenza Epidemic of 1957–1958 in Sweden. Vaccination Trials]** *Nordisk Med.* 1958, Nov. 27, v. 60, No. 48, 1706–10, 5 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"The antibody responses of volunteers inoculated with falling dilutions of a monovalent formalinised Asian-influenza vaccine, prepared at the State Bacteriological Laboratory in Stockholm, were determined by the haemagglutination-inhibition test. In spite of the low haemagglutinating capacity of the vaccine strain (A/Singapore/1/57) even extremely small doses of the vaccine (15—50 haemagglutination units per ml) gave 11—22% serologically positives after one and 55% positives after two injections. A dose of 1,500 haemagglutination units produced an almost hundred per cent antibody response after one injection.

"Another vaccine, preparation, containing a high haemagglutination titre line of the same influenza virus strain, was tested in a field trial in more than one thousand recruits, in an attempt to perform a direct titration of the protective effect of the vaccine. The protection rates found for a dose of 2,000 haemagglutination units were 69—86% for two and 57—78% for one vaccine injection. The corresponding figures for

two doses of 400 haemagglutination units were 45—54% and for one dose 29—45%protection. All effects were statistically significant.

"The results of the two trials were used for a critical discussion of the current methods of vaccine potency tests as well as for an evaluation of the quantitative relation between the antibody-stimulating and the protective effects of vaccination against influenza."

OHELA, K. & KAIPAINEN, W. J. Influensadödlighten i Finland 1957. [**Influenza Mortality in Finland in 1957**] *Nordisk Med.* 1958, Nov. 27, v. 60, No. 48, 1700–701, 2 figs.

The English summary appended to the paper is as follows:—

"The Asiatic influenza epidemic was spreading in Finland at the end of September 1957. From South-western Finland it had extended throughout the country by the beginning of November. In December the figures for the incidence of new cases began to show a decrease. Influenza morbidity figures based on notifications by physicians were many times those for earlier years and the total number of cases is estimated to be at least 700,000. According to the death certificates, a total of 1,322 persons died in the autumn 1957 epidemic. Among this total influenza was the sole cause of death in 478 cases; in the rest one or more additional diseases were involved. A considerable proportion of the fatal cases were children under 5 and old people over 65 years of age."

KÖRLOF, B., MÖRNER, J., ZETTERBERG, B., BÖTTIGER, M., HELLER, L., JOHNSSON, T. & BACKELIN, B. Influensaepidemien i Sverige 1957–1958. Epidemiologi. [**The Influenza Epidemic of 1957–1958 in Sweden. Epidemiology**] *Nordisk Med.* 1958, Nov. 27, v. 60, No. 48, 1704–6, 7 figs.

The English summary appended to the paper is as follows:—

"Asiatic influenza occurred in epidemic form in Sweden during the period September 1957 to April 1958, with peak morbidity in November 1957. It is estimated that roughly one million persons were affected, the highest incidence being recorded among school children and Army personnel.

"The over-all mortality figures are not yet known. The material studied suggests that the number of deaths from the influenza or its complications was higher in children below the age of 16 years and in persons over 61 than in the intermediate age groups. The cause of death was in the majority of cases pneumonia due to bacteria or to a combination of bacteria and the Asiatic influenza virus. The bacteria most commonly found on autopsy were Staphylococcus aureus pyogenes and Escherichia coli."

KANAGARATNAM, K. **Influenza Epidemic in Singapore, 1957.** *Pub. Health.* 1958, July, v. 72, No. 4, 143–6.

In the beginning of May, 1957, an unknown fever was reported from a small island just south of the main island of Singapore. Clinical investigations supported by virus studies defined the fever as influenza and since there were many contacts with the main island by 5th May the disease had reached epidemic proportions there. The outbreak reached its peak about the middle of May and by the last days of that month it had come to an end. It was not possible even to guess the real incidence but there is no doubt a substantial proportion of the population was affected and 77,211 cases were seen in Government and City Council clinics while 326 were admitted to hospital. Influenza and its complications accounted for 28 deaths during the relevant period, 22 from influenzal or haemorrhagic pneumonia, and 6 from myocarditis or heart failure.

The main causative virus has since been identified as a new strain of type A and has been called influenza A Singapore 1/57 but other strains were also isolated. The disease itself conformed to that as usually described, tracheitis and bronchitis being the commonest complications. A fair number of relapses occurred, studies in the police force showing that out of a total of 1,858 cases relapse presented in 256 (13%). Males and females were equally affected, there was no predilection for any age group, and Asians were more heavily attacked than Europeans. As regards prevention no quarantine measures were taken against inward or outward passengers, ships or aircraft. Schools were closed at the peak period and the public were warned to keep away from crowded places. Elective surgery was reduced to a minimum to release staff for treatment, school health and maternal and child health centres became centres for treatment of influenza, two additional travelling dispensaries were put on the road and the government assisted with drugs, equipment and facilities. The author is of the opinion that the epidemic started in Japan and followed the shipping lines to the great ports of Hongkong, Singapore, Manila, Djakarta, and Saigon and thereafter into the hinterland. *A. Joe*

BEAVEN, D. W. & PLATTS, W. M. **The 1957 Influenza Epidemic. An Analysis of Patients admitted to Hospital with Respiratory Tract Infection.** *New Zealand Med. J.* 1958, Feb., v. 57, No. 317, 32–37, 1 fig.

In August 1957 an explosive epidemic of influenza due to the Asian strain of virus type A occurred in Christchurch, New Zealand. The peak was reached in the first week of September and in 4 weeks from its beginning it had abated. This report concerns all patients, numbering 216, with respiratory tract infection admitted to hospital over the epidemic period. The maximum age incidence of both consolidation and upper respiratory infection without pneumonia was in the first 10 years of life, 41% of patients falling into this group. As the epidemic progressed patients in the 60–80-years age-group formed an increasing percentage of the admissions and eventually those over 70 years of age were 17% of the total. There was no significant difference in sex.

Radiological evidence of pneumonia was found in 150 patients, this being bilateral in 36. *Streptococcus pneumoniae* was the main pathogenic secondary invader,

being the main organism cultured in 65 cases, and also the organism giving the second heaviest growth in the majority of cultures. In 32 instances *Staphylococcus aureus* was the main organism but in only 8 did it appear in pure culture. However, 5 of these patients died. *Str. viridans* was found in 58 instances and *Haemophilus influenzae* in 18. A stained sputum was found to be a good guide to treatment for staphylococci were unlikely to be the main pathogen unless they predominated in the direct smear.

9 patients died, 4 of them young adults succumbing within 36 hours of hospital admission from overwhelming staphylococcal infection. Penicillin proved to be the treatment of choice in over 60% of the admissions. *A. Joe*

LANGMUIR, A. D. **Asian Influenza in the United States.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 483–92, 5 figs.

The pandemic of Asian influenza during 1957 was due to a major antigenic shift in the A virus. It had been predicted that if such a shift occurred the spread would be world wide within a year. This is what happened when the new strain reached the Western world from Northern China through Hongkong. Fortunately it was only slightly more severe than the A prime epidemic of 1953.

Asian influenza began to spread from California in late June through delegates to a conference in the Middle West. There was no dynamic spread, however, until the opening of the schools in late August. The peak of the epidemic in the United States was in the third week of October, after which there was a rapid steady decline to almost zero by the end of November. A so-called "second wave" in January, February and March 1958 was evidenced by a renewed sharp increase in mortality from influenza pneumonia, especially in the age-groups 65 years and over; but this was not accompanied by any clear-cut increase of influenza morbidity in the population generally. No explanation for this unusual phenomenon has yet been found.

It is generally expected that the Asian strain will dominate the influenza picture for the next decade, with epidemics every few years. There may, however, be surprises. The 1957 pandemic may prove to be a unique phenomenon like those of 1889 and 1918.

H. Stanley Banks

DAUER, C. C. **Mortality in the 1957–58 Influenza Epidemic.** *Pub. Health Rep.* Wash. 1958, Sept., v. 73, No. 9, 803–10, 3 figs.

The 1957 outbreak of Asian influenza in the United States followed a similar pattern to that experienced in England and Wales. In both countries the number of deaths from influenza and pneumonia in the large cities rose rapidly to a peak, subsided, and then rose again. The interval between the 2 peaks was about 3 months. In the United States the epidemic appeared about 1 month later than in England and Wales. In both countries children experienced a high incidence. During the peak in October the United States National Health Survey estimated the respiratory disease rate per 1,000 persons per week to be 28 at ages under 5 years, 111 at ages 5–19, 16 at ages 20–64 and 9 at ages 65 years and over.

A comparison with other influenza years in America showed that the mortality was only moderate, but that the period of increased mortality extended over a period of about 6 months instead of the usual 3–4 months. The death rate from influenza and pneumonia was 66·6 per 100,000 at the peak of the outbreak in November. The elderly were mainly affected; the death rate from influenza and pneumonia at ages 65 years and over was 405 per 100,000 in November 1957.

As usual during an influenza year there was a general rise in mortality, but influenza formed a smaller proportion of the excess deaths than in other epidemics. The author examined this feature but was unable to explain the large excess of deaths from other causes. About half of the excess deaths were attributed to cardiovascular diseases, and a rise in these causes was not unexpected since most of the excess deaths were among older persons. *W. J. Martin*

DAVENPORT, F. M. & HENNESSY, A. V. **The Clinical Epidemiology of Asian Influenza.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 493–501, 5 figs. [16 refs.]

The epidemiology of Asian influenza was investigated to see whether the new Asian strain was producing major changes in the clinical picture and mortality of the disease. In Manila and Santiago the usual U-shaped curve of mortality was found, impliciting significantly the extremes of life. In Chile the attack rate was the highest since 1918–19, and the number of deaths from influenza and pneumonia was 5·1 times greater than in the same period of the previous year. The fatal cases fell into 3 groups: (1) those suffering in addition from a chronic illness, debility or pregnancy, (2) those attacked by antibiotic-resistant staphylococcal pneumonia (approximately 50% of the fatal cases) and (3) a few cases associated with haemorrhagic or membranous pneumonia. These and other investigations suggested that Asian influenza did not behave like a new disease, and that immunity to it, as to other strains of the virus, was probably related to composite antibody built up through multiple exposure to many antigenic variants of influenza A. In persons over 65 years of age, however, specific antibody to the Asian strain played a part, though (in the authors' judgment) a subordinate one.

The authors consider that the experience of Asian influenza has added clear support for interpretations made from earlier observations on age distribution of influenza antibodies in the population and their relation to initial exposure and immunity.

H. Stanley Banks

BENDKOWSKI, B. **Asian Influenza (1957) in Allergic Patients.** *Brit. Med. J.* 1958, Nov. 29, 1314–15.

The author is a general practitioner and also a clinical assistant to the Allergy Clinic, North Lonsdale Hospital, Barrow-in-Furness. He knew and had treated the allergic patients in his group practice and

he was able to study their response to Asian influenza in 1957 as compared with the response of non-allergic patients. He observed 124 allergic patients ill with influenza, 59 non-allergic patients from allergic families and 161 non-allergic patients from normal families. The allergic patients suffered much more severely from influenza than the non-allergic patients; 14 out of 124 developed pneumonia compared with 8 out of 161, and 47 had attacks of bronchitis with asthma compared with none in the non-allergic group. There was a tendency among non-allergic patients from allergic families to develop respiratory complications more readily than those from normal families. The incidence of after-effects, mainly chronic cough and asthma, was higher in allergic patients. *A. B. Christie*

BUEBENDORF, D. P., CARSON, T. E., COOPER, N. R., MOYNIHAN, M. J. & YANKEE, R. A. **Asian Influenza: a Study of 150 Persons during the 1957 Pandemic.** *Yale J. Biol. & Med.* 1958, Sept., v. 31, No. 1, 14–28, 2 figs.

3 groups of 50 patients were studied in the autumn 1957 influenza outbreak at Yale University School of Medicine. One group of students were given 2 intradermal injections of 0·1 ml. Asian influenza vaccine containing 200 CCA units per ml. before the outbreak; a second group of students from the same centre were unvaccinated, and a third group of 50 patients came from a separate institution. Blood for serological titration was taken before and after injections and again after any subsequent illness in the first group, in the other 2 groups before the epidemic and after the epidemic or after any illness. An influenza-like illness occurred in 3 out of 50 vaccinated students, in 20 out of 50 students from the same centre and in 33 out of 50 from the third group; the illness was confirmed serologically as influenza in 1 out of 3, 16 out of 20 and 28 out of 33 patients in the 3 groups. Neither complement fixation nor haemagglutination inhibition titres detected all the illnesses or subclinical infections; thus of 47 vaccinated patients without clinical illness 12 showed a 3-fold rise by complement fixation titration, 8 by haemagglutination inhibition titration and 6 by both. The results do seem to show that considerable protection was given by the 2 intradermal injections during the autumn outbreak.

A second wave of influenza-like illness occurred in the 2 Yale Medical School groups in the spring of 1958 and the highest incidence appeared to be in the vaccinated group, of whom 25 reported influenza-like illness in the second wave; 13 of these patients had shown a serological response in the original study. Of the unvaccinated Yale group, 14 reported illness during the second wave and 5 of these had serological evidence of infection in the first wave, 2 of whom had symptoms during both epidemics. [The figures are of great interest though obviously too small for valid deductions.] *A. B. Christie*

BASHORE, S. M., BOSNIAK, M. A., AKKA, R. I. & FLANIGAN, W. J. **Asian Influenza. Review of 1,264 Unselected Cases.** *U.S. Armed Forces Med. J.* 1958, Nov., v. 9, No. 11, 1569–79, 2 figs.

WALSH, J., BURCH, G. E., WHITE, A., MOGABGAB, W. & DIETLEIN, L. **A Study of the Effects of Type A (Asian Strain) Influenza on the Cardiovascular System of Man.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 502–28, 8 figs. [55 refs.]

This is a long, detailed paper on the clinical evaluation of 34 patients with Asian influenza. Extensive laboratory examinations and cardiovascular investigations were made on all of them. At the height of the illness approximately three-fourths of the patients were found to have digital vasoconstriction as well as abnormalities of the T wave in the standard electrocardiogram. These changes were, however, transitory and disappeared with convalescence. In spite of intensive search for clinically significant cardiovascular complications of influenza, none was found in the 30 patients of the first group, 10 of whom had been admitted to hospital because of the severity of their pulmonary infection, or because they did not have adequate home care. The second group of 4 patients with cardiovascular complications are described in detail; the diagnosis in all was confirmed virologically. 2 had rheumatic heart disease with mitral stenosis, and 1 of these suffered from cardiac insufficiency during the influenzal attack. Patient No. 3 was pregnant and suffered from acute pulmonary oedema. No. 4 experienced a severe episode of acute rheumatic pancarditis complicated by congestive heart failure, although evidence of streptococcal infection was meagre. In this case the influenzal infection seemed to be of considerable importance in producing the cardiac manifestations. *H. Stanley Banks*

OSWALD, N. C., SHOOTER, R. A. & CURWEN, M. P. **Pneumonia complicating Asian Influenza.** *Brit. Med. J.* 1958, Nov. 29, 1305–11. [38 refs.]

Of 165 cases of influenzal pneumonia occurring in 10 London teaching hospitals in the autumn of 1957, 20 were caused by staphylococci. To these 20, 135 cases of staphylococcal pneumonia occurring in other hospitals in or near London were added, and the total 155 cases of staphylococcal pneumonia were compared with the 145 cases of non-staphylococcal pneumonia. The mortality in the staphylococcal group was 28% and this did not vary according to age; in the non-staphylococcal group the mortality was 12% and this varied from 0 in the 0–14 age group to 26% in the group aged over 55. Severity was assessed also on clinical grounds, length of stay in hospital, duration and height of temperature and radiological findings; 3 or more lung zones were shown to be involved in 37% of the staphylococcal cases but only in 19% of the others; lung abscesses were present in 21 out of 155 staphylococcal cases but in only 2 out of 145 non-staphylococcal cases. *Streptococcus pneumoniae* and *Haemophilus influenzae* were the commonest pathogens in the non-staphylococcal group, though in 50% no pathogens at all were found.

2 features were prominent in the clinical aspects of the severe cases, toxaemia and respiratory obstruction.

Adrenal steroids may have been of some use in combating overwhelming toxaemia, and some form of tracheo-bronchial intubation may have been indicated for respiratory obstruction. A variety of antibiotics were used but no valid conclusion could be drawn. Of staphylococci isolated within 4 days of the patient's admission, 49% were resistant to penicillin and 22% to tetracycline compared with 93% and 74% of those isolated more than 4 days after the patient's admission or from patients who contracted their influenza in hospital. *A. B. Christie*

KAPILA, C. C., KAUL, S., KAPUR, S. C., KALAYANAM, T. S. & BANERJEE, D. **Neurological and Hepatic Disorders associated with Influenza.** *Brit. Med. J.* 1958, Nov. 29, 1311–14. [12 refs.]

Of 9,459 patients suffering from influenza and admitted during 1957 to military hospitals in South India, 30 developed signs of neurological and hepatic involvement. These signs usually followed an afebrile period after a typical attack of influenza and were ushered in by incessant vomiting, delirium, boisterousness and coma. 17 patients died and postmortem examination showed typical signs of influenzal changes in the lungs; influenza virus A was isolated from the lungs in 5 cases. The liver showed a variable and indefinite picture. Changes in the brain varied from moderate to severe congestion with petechial haemorrhages in the white matter; there was diapedesis of cells and in a few cases neuroglial proliferation; 1 case showed neurone degeneration and clinically the patient had extensive paralysis of the muscles of trunk and limbs; influenza virus A was isolated from the brain in this case. Raised serum bilirubin was present in one-third of the cases but was never high enough to account for the symptoms. It appears likely that the syndrome is closely related to infection with influenza virus but the exact relationship is not clear. *A. B. Christie*

MEIKLEJOHN, G. & MORRIS, A. J. **Influenza Vaccination.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 529–35, 4 figs.

Certain field trials at an Air Force Base in Colorado showed that with specific Asian influenza vaccines the antibody response to a single injection was far less satisfactory than that obtained in the past with comparable vaccines made from other strains. It is clear that the population had had insignificant prior experience of the dominant antigens of the Asian strain and that, accordingly, 2 injections at least would be necessary for a really satisfactory antibody response. The first controlled study of men vaccinated with 200 chicken cell agglutinating (CCA) units of the Asian strain at the end of July 1957 showed a protection ratio of 2·5 to 1 of the controls. In the second controlled study, in which an injection of 400 CCA units was given on 24 September (when the epidemic had already started), the protection ratio was 3·6 to 1 when account was taken only of the period from the 10th day after vaccination. [In similar former studies with the A-prime strain the protection ratio was 5·5 to 1.]

From these studies the hypothesis that only a limited number of major families of influenza viruses exist is considered to be strengthened. If such families were limited to 4, or possibly 5, for influenza A, then basic immunization could be relatively easily provided against influenza A by preparing vaccines containing antigens of all these major families. Similarly a polyvalent vaccine might be prepared against influenza B. [It remains to be seen whether this American conception of a polyvalent vaccine for immunization against influenza can be realized in practice.]

[See also this *Bulletin,* 1958, v. 33, 730.]

H. Stanley Banks

VAN DER VEEN, J. & VAN DER PLOEG, G. **An Outbreak of Pharyngoconjunctival Fever caused by Types 3 and 4 Adenovirus at Waalwijk, the Netherlands.** *Amer. J. Hyg.* 1958, Sept., v. 68, No. 2, 95–105, 2 figs. [27 refs.]

Clinical, epidemiological and laboratory studies on an outbreak of pharyngo-conjunctival fever are reported. The outbreak started during the first week of July 1957 and reached a peak during the 2 following weeks. The symptoms observed included fever, headache, pharyngitis, conjunctivitis, rhinitis and cervical adenitis. Epistaxis occurred in about 40% of patients and gastro-intestinal symptoms (nausea, vomiting and diarrhoea) were observed in almost one-third. Adenoviruses were isolated in HeLa cell cultures from 83% of 75 patients from whom specimens were obtained. Viruses were isolated from stools more frequently than from throat swabs. Type 3 virus was isolated from 46 patients, type 4 from 11, type 5 from 2 and types 2, 7 and 9 each from 1 patient. Acute and convalescent sera from 35 patients were tested by complement fixation with adenovirus type 4 antigen and the results were in good agreement with virus isolation attempts. Serum-neutralization tests were performed with 16 serum pairs from patients from whom adenovirus types 3 or 4 had been isolated. Homologous serum-neutralizing antibody rises were observed in all cases, and 4 of 12 patients infected with adenovirus type 3 showed in addition heterotypic antibody rises against adenovirus type 4. Some evidence is presented suggesting that such heterotypic responses may have been due to mixed infections.

Epidemiological data were obtained from the study of 92 families, including 107 patients investigated by laboratory methods. 63% of adenovirus infections occurred among children aged 8–14 years and the incidence of infection in boys was higher (about two-thirds of the cases) than in girls. Evidence suggesting that swimming played a part in the spread of infection is presented. *H. G. Pereira*

FUKUMI, H., NISHIKAWA, F., NAKAMURA, K., WATANABE, T. & KITAYAMA, T. **Further Studies of the Cases associated with Adenoviruses.** *Japanese J. Med. Sci. & Biol.* 1957, Dec., v. 10, No. 6, 407–18, 2 figs. & 2 pls. [18 refs.]

GUNDELFINGER, B. F., HANTOVER, M. J., BELL, J. A., LOOSLI, C. G. & ROWE, W. P. **Evaluation of a Trivalent Adenovirus Vaccine for Prevention of Acute Respiratory Disease in Naval Recruits.** *Amer. J. Hyg.* 1958, Sept., v. 68, No. 2, 156–68, 5 figs. [31 refs.]

A vaccine containing formalin-inactivated adenovirus types 3, 4 and 7 was administered to 20% of 14,000 recruits entering naval training centres between January and April 1956. The remaining 80% of recruits served as controls. Antigenicity of the vaccine was demonstrated by antibody rises against each of the 3 virus types in random groups of vaccinated subjects. Prevalence of adenovirus type 4 infections during the study period was shown by the results of serological tests and virus isolations from random groups of unvaccinated recruits [this *Bulletin*, 1956, v. 31, 1194]. The protective effect of vaccination was evaluated by the frequency of reported febrile respiratory illnesses which in vaccinated recruits was less than one-half that of the control group. Protection of vaccinated subjects against febrile respiratory illness became manifest approximately 2 weeks after vaccination. Vaccination caused no significant reduction of reported afebrile respiratory illness.

Adenovirus type 4 was isolated from throat swabs of 8% of vaccinated and 13% of unvaccinated patients hospitalized with respiratory disease.

It is concluded that adenovirus vaccines can be of great value in the control of respiratory disease in military recruits, but further study is required before this vaccine can be recommended for the general public.

H. G. Pereira

TYRRELL, D. A. J. & BYNOE, M. L. **Inoculation of Volunteers with J. H. Strain of New Respiratory Virus.** *Lancet.* 1958, Nov. 1, 931–3, 2 figs.

The JH virus, an agent isolated by PRICE [this *Bulletin*, 1958, v. 33, 621] from patients with mild respiratory disease resembling the common cold, was administered intranasally to 58 volunteers kept in strict isolation. A virus inoculum consisting of fluids from 12th passage in monkey kidney cultures was administered after dilution to 1 in 100 and 1 in 1,000 (containing about 1,000 and 100 TCD50) to groups of 6 and 10 volunteers respectively. No colds developed in any of these volunteers, but virus identified as JH was isolated from respiratory secretions from 1 volunteer in each of the 2 groups. A 1 in 6 dilution of 1 of these virus-containing secretions was administered to 11 volunteers and gave rise to 5 infections, demonstrated by virus isolations, 2 of which were accompanied by common cold symptoms. Subsequent passages of infective respiratory secretions to volunteers gave rise to a small proportion of colds, from some of which no virus could be recovered. Several explanations for these findings are discussed, and it is tentatively suggested that some of the colds observed may have been due to a secondary agent activated by infection with JH virus.

Evidence of multiplication of JH virus in the respiratory tract of volunteers is presented. No correlation between serum neutralizing antibody levels and susceptibility to infection by JH virus was observed and no JH antibody rises could be detected in pre- and post-inoculation sera from infected or uninfected volunteers. Evidence suggesting that an agent serologically related to JH virus is present in England was provided by the result of a serological survey.

H. G. Pereira

JACKSON, G. G., DOWLING, H. F. & ANDERSON, T. O. **Neutralization of Common Cold Agents in Volunteers by Pooled Human Globulin.** *Science.* 1958, July 4, v. 128, 27–8.

Filtrates of nasal secretions from patients with common cold were administered intranasally to volunteers, after incubation at 37°C. for 30 minutes with (a) pooled human globulin at a final concentration of about 8·0% protein, (b) boiled human globulin concentrated to 12·0% protein, (c) human serum albumin, or (d) Hanks salt solution. The proportion of colds observed among volunteers given filtrates incubated with salt solution (65 volunteers), boiled globulin (20 volunteers) or serum albumin (18 volunteers) varied between 44·5 and 55% and differed significantly ($p<0·001$) from the value of 10·2% observed among 59 volunteers given filtrates incubated with unheated human globulin. Pooled human globulin was also shown to delay and modify the common cold symptoms in volunteers who were not completely protected. Possible explanations for the lack of lasting resistance against the common cold are discussed.

H. G. Pereira

KRINGELBACH, J. & WINGE, J. **Staphylococcal Pneumonia in Infancy and Childhood. Annotation.** *Danish Med. Bull.* 1958, May, v. 5, No. 4, 159–60.

Based upon the literature available from foreign sources, the authors give a description of the clinical findings in staphylococcal pneumonia and of its treatment. They point out that the majority of cases occur in infants up to 4 months of age, 2 clinical types being distinguishable. In one there is an acute fulminating form following a trivial upper respiratory infection, producing death within a few days of onset. The other follows a more prolonged and benign course and is recognized by absence of reaction to sulphonamides or penicillin, the age of the child, radiological findings and the occurrence of pyopneumothorax and empyema. Diagnosis is verified by the demonstration of staphylococci in pleural fluid, blood, or in the products of lung puncture. In treatment tetracyclines, supplementary oxygen and surgical measures in pleural complications are required and, late in the disease, possibly lung resection in bronchiectasis, chronic lung abscess, or relapsing atelectasis. A retrospective review of all cases of pneumonia occurring in a Danish paediatric department over 2 years reveals that staphylococcal pneumonia constitutes approximately 6% of all cases of pneumonia and accounts for half the pneumonia deaths.

A. Joe

LEIBOWITZ, S. **Hospital Precautions against Spread of Acute Viral Hepatitis.** *J. Amer. Med. Ass.* 1958, July 19, v. 167, No. 12, 1474–6. [11 refs.]

Isolation precautions should be taken in all hospitals in which cases of either infectious or serum hepatitis are nursed. The nursing precautions appropriate are of the standard usually adopted for nursing typhoid fever; details are given. In addition, anyone engaged in drawing blood, making injections or handling material liable to faecal contamination should take the additional precautions listed. Blood transfusion and pooled plasma injections should be avoided or reduced to a minimum. Gamma globulin 0·02–0·06 ml. per lb. of body weight should be given to certain contacts, including children, pregnant women, debilitated persons, those exposed during an epidemic, and to medical, nursing and other staff unduly exposed.

H. Stanley Banks

MASON, W. R., Jr. & ADAMS, Elizabeth K. **Infectious Mononucleosis. An Analysis of 100 Cases with particular attention to Diagnosis, Liver Function Tests and Treatment of Selected Cases with Prednisone.** *Amer. J. Med. Sci.* 1958, Oct., v. 236, No. 4, 447–59. [90 refs.]

It is generally assumed that infectious mononucleosis and glandular fever are the same, but some workers have pointed out that glandular fever occurs in children and infrequently presents a significant pharyngitis, whereas infectious mononucleosis occurs in adults and pharyngitis is a common symptom. The cases studied by the authors were in young adults attending a college health centre.

The heterophile agglutination test is regarded by some as a *sine qua non* of diagnosis; others attach less significance to it. The authors of this article consider that the reliability of this test as commonly performed has probably been somewhat over-rated. There is good reason to believe that seronegative cases do occur even with absorption studies. Moreover there is a lack of agreement in regard to the interpretation of the test. In the absence of absorption studies the diagnostic titre varies, according to the literature, from 1: 56 to 1: 1,792. After guineapig absorption some say the titre should not drop more than 3 tubes or to no less than $\frac{1}{8}$ of the non-absorbed titre; others may accept levels of any degree after absorption. There is no doubt but that absorption tests are of definite value and that they may increase the value of the test, but they are not infallible. In the course of the studies here recorded it was found that a titre of 1: 112 without absorption was the minimum that could be considered positive. The serum-cell test mixtures were never refrigerated but were incubated at room temperature for at least 2 hours. When absorption studies were made the test was considered positive if the titre after guineapig absorption did not fall to less than $\frac{1}{8}$ of the original titre and if the titre after beef cell absorption fell significantly below this level, usually to zero or nearly so.

The significance of the haematological changes has, like the heterophile test, been the subject of disagreement. The authors consider the characteristic alteration of the lymphocytes highly important in diagnosis and often more useful than the heterophile test. Both, however, are unspecific. They consider that the blood picture of infectious mononucleosis is characteristic when 50% or more of the total leucocytes are lymphocytes and when 15% or more of the total leucocytes are atypical lymphocytes. In the beginning, a patient with infectious mononucleosis may have a completely normal total and differential white cell count, but the blood smear may change very significantly within as short a period as 24 hours, showing an increase of lymphocytes and atypical cells. In the case of fever of undetermined origin or of posterior cervical adenopathy or of exudative pharyngitis in which the possibility of infectious mononucleosis is entertained it is important to repeat the blood smear every day or two.

Liver function tests were performed on 62 of the patients and it was found that the thymol turbidity test was not often increased; bromsulphthalein, however, was commonly positive. It generally became positive early, usually about the beginning of the second week or about the time the heterophile test became positive, then it tended to revert to normal fairly promptly, that is within 7 to 10 days. The cephalin flocculation test usually became positive later than the bromsulphthalein and had a tendency to persist for a longer time, even 2–3 months. It was found helpful in judging the time when the patient should be allowed to become ambulatory. Some alteration of liver function seems to be characteristic, but from a clinical standpoint there is a difference between the hepatitis of an average case of infectious mononucleosis and that of an average case of infective hepatitis. None of the patients showed jaundice; serum bilirubin tests were carried out on 14 patients and of these, 3 showed a slight elevation of 1–2 mgm. per 100 ml.

There is no specific therapy, but rather encouraging results were obtained by treatment of 17 patients with prednisone. The hormone did not obscure laboratory tests and there were no complications that could be attributed to it but it did not appear to shorten the course of the disease. It was administered in small doses of 20 mgm. daily for 1–3 days, then tapered off by reduction of 5 mgm. on each succeeding day.

Infectious mononucleosis is not really a protean disease but the complications are unusual and infrequent and have given the disease the reputation of being protean and unpredictable. The fact that symptoms of complications may precede the usual clinical and laboratory manifestations of the primary disease has contributed further to this concept.

P. A. Clearkin

BENDER, C. E. **Interpretation of Hematologic and Serologic Findings in the Diagnosis of Infectious Mononucleosis.** *Ann. Intern. Med.* 1958, Oct., v. 49, No. 4, 852–65, 3 figs. [18 refs.]

The observations in this paper embody the results of experience gained by treatment of 600 carefully studied

cases of infectious mononucleosis seen for the most part in a university population.

Differential white cell counts in blood from patients suffering from infectious mononucleosis were regularly characterized by lymphocytosis, high atypical lymphocyte counts and a heterophile antibody titre of 1 : 56 or more as well as by clinical manifestations. The lymphocyte count was not a transitory manifestation but was present day after day during the acute phase and early convalescence. From the laboratory standpoint the basic screening procedure is identification of atypical lymphocytes as these are practically pathognomonic of the disease. The absolute total white cell count ranged from 5,100 to 26,500 per cmm. and the absolute atypical lymphocyte range count from 1,400 to 13,500 cells, the average being 4,884. Only in rare instances were atypical lymphocytes less than 20%.

Records of 200 patients studied early in the disease showed that in only 1 instance was the neutrophile count lowest in the early stages; in some, the lowest count coincided with the peak of the fever but the majority showed the lowest count about the time of return of the temperature to normal.

The minimum figure of the diagnostic titre of antibodies in the heterophile test with unabsorbed serum was 1 : 56; after absorption with guineapig kidney 1 : 28, at least 1 : 14, and after absorption with beef cell antigen no agglutination should occur. In general, a differential absorption formula showing little or no absorption of the antibody by guineapig antigen, and complete absorption by beef cell antigen, is diagnostic. Readings were made macroscopically after standing for 2 hours at room temperature. False high titres are given by standing overnight in the refrigerator as required by the original Paul-Bunnell reaction.

In practice it is seldom necessary to do differential absorption tests. The main indication is a positive presumptive test unaccompanied by typical blood changes. Other indications are an incomplete clinical syndrome, some atypical clinical sign and persistently low titres, especially in the presence of severe systemic disease. In the presence of a diagnostic blood picture differential absorption tests are reassuring rather than helpful. *P. A. Clearkin*

PHILIPS, V. K. **Acute Meningococcaemia with Symmetric Peripheral Gangrene: Report of a Case with Recovery.** *Ann. Intern. Med.* 1958, Apr., v. 48, No. 4, 864–71, 6 figs. [17 refs.]

The patient, a soldier aged 20, suffered from a severe meningococcaemia, which, in addition to the usual features of the Waterhouse-Friderichsen syndrome, showed a septic, occlusive gangrene of the fingers of both hands and toes of both feet. Immediate improvement and eventual recovery was obtained by the use of sulphonamide and penicillin, although the organism was later found to be insensitive to the latter. Intravenous hydrocortisone in massive doses was applied as well as supportive therapy. It is recorded that partial amputation of the distal phalanges of the right great toe and of the left index finger were required, all other areas having healed normally. *A. Joe*

PEROU, M. L., FIELDING, R. T. & NELSON, H. M. **Leptomeningitis due to *Gaffkya tetragena*. Report of a Case treated with Chloromycetin and a Brief Review of the Literature.** *J. Pediatrics.* St. Louis. 1958, Oct., v. 53, No. 4, 484–8, 3 figs. [24 refs.]

This is an account of a rare form of acute meningitis of which only 16 cases have been published—all French or American. The age range of the published cases was 12–58 years, and the male/female ratio about 3 to 1. The onset is sudden with symptoms of severe acute meningitis, the duration 1–5 weeks or longer, and the outcome at least 75% fatal unless treatment with an appropriate antibiotic is given. The spinal fluid may be purulent, or non-purulent with high protein and low sugar content (as in the present case). In the case described, a boy of 12, the fluid was clear, but smears showed scattered extracellular Gram-positive cocci with a tendency to tetral arrangement. Culture in brain heart infusion revealed growth on the 4th day, and subculture on blood agar yielded the typical Gram-positive cocci of *Gaffkya tetragena*, arranged generally in tetrads.

Specific treatment depends on the antibiotics to which the strain cultivated is found to be sensitive. In this case these were chloramphenicol, erythromycin, and dihydrostreptomycin. Tentative treatment with penicillin and streptomycin had been given for 3 days without any success when chloramphenicol treatment was started. The response to the latter was very rapid; within 2 days the boy became conscious, and sat up in bed temporarily afebrile. Progress was uninterrupted, and there were no sequelae when he was seen 21 months later. *H. Stanley Banks*

BENEDIKTSSON, G., GUDNADÓTTIR, M. & PÉTURSSON, G. En epidemi af serøs meningitis i Island. [**An Epidemic of Aseptic Meningitis in Iceland**] *Nordisk Med.* 1958, July 31, v. 60, No. 31, 1099–1100. English summary.

During the summer and autumn of 1956 an epidemic of serous meningitis occurred in Iceland, and the authors give an account of clinical observations made on 29 patients suffering from the disease who were admitted to hospital. The age of the patients ranged from 3 months to 45 years; all had fever with a temperature of 38°–40°C., usually lasting for 2–5 days and in 3 cases up to 10 days, and also headache and nausea. In some cases there was vomiting, weakness and muscle pains. All patients had neck rigidity, 4 a positive Kernig sign, 18 had infection of the pharynx and 5 had cervical lymphadenitis. The cerebrospinal fluid showed a lymphocytic pleocytosis of up to 1,500 cells per cmm., and the protein content was increased in 12 patients. The illness was relatively mild and there were no fatal cases. A relapse occurred in 8 patients after an afebrile period of 1–2 days, and 3 of them suffered from 2 relapses. 14 strains of cytopathogenic virus were isolated in monkey kidney cell cultures, 7 from 29 specimens of stool and 7 from 22

specimens of cerebrospinal fluid; 5 strains were neutralized by convalescent-phase sera, and a diagnosis of ECHO-9 meningitis was established by neutralization tests with reference antisera. 2 strains were pathogenic for infant mice after passage in tissue culture.

D. J. Bauer

JUST, M. & BERGER, E. Ätiologische Untersuchungen bei 67 abakteriellen Meningitiden und Meningoencephalitiden des Jahres 1957. Unter Berücksichtigung der Poliomyelitisschutzimpfungen in Basel 1957. [**Aetiological Investigations on 67 Cases of Abacterial Meningitis and Meningo-Encephalitis in 1957, in regard to Poliomyelitis Vaccination in Basle in 1957**] *Schweiz. med. Woch.* 1958, May 31, v. 88, No. 22, 542–6. [14 refs.]

Serological and virological examinations have been carried out on 67 children admitted to hospital with a diagnosis of non-bacterial meningitis or meningoencephalitis in Basle in 1957. A diagnosis of poliomyelitis was established in 18 instances by isolation of virus, and in 2 further instances by the demonstration of a diagnostic rise of antibody titre; 18 patients had not been vaccinated, and 2 with meningeal symptoms only had received 2 doses. One child showed a diagnostic rise in titre against Coxsackie B3 virus and a lesser rise of poliomyelitis neutralizing antibody, and Coxsackie B3 virus was isolated from the stools; the patient was considered to be suffering from a mixed infection. 7 patients had poliomyelitis complement-fixing antibody without a rise in titre of neutralizing antibody, in 29 cases a diagnosis of poliomyelitis could not be established and the 10 remaining patients were shown to be suffering from mumps or ECHO-9 infection.

D. J. Bauer

WIESMANN, E., HEGGLIN, R. & WIESMANN, W. Zur Ätiologie und Differentialdiagnostik der Meningitis serosa. Klinische und virologische Untersuchungen. [**The Aetiology and Differential Diagnosis of Serous Meningitis, Clinical and Virological Investigations**] *Schweiz. med. Woch.* 1958, July 12, v. 88, No. 28, 679–83, 4 figs. [11 refs.]

By means of virological examinations carried out on 49 patients suffering from non-paralytic serous meningitis admitted to the St. Gallen Hospital, Switzerland, in 1957, the causative agent was identified as poliomyelitis virus in 1 instance, ECHO-6 in 4, ECHO-9 in 7, other ECHO types in 6, Coxsackie B in 13, mumps in 3, *Rickettsia burneti* in 1 and a leptospire in 11 instances; in 3 cases an aetiological diagnosis could not be made. A similar examination of 14 persons suffering from paralytic disease yielded 9 strains of poliomyelitis virus, 1 strain of ECHO-6 and 3 strains of Coxsackie B virus. Poliomyelitis and ECHO infections could not be differentiated on clinical grounds, but cases of Coxsackie B infection could usually be recognized by the presence of lymphadenitis and enlargement of the spleen. Histories are given of 2 cases of paralytic illness due to ECHO virus infection.

D. J. Bauer

PUBLIC HEALTH LAB. SERVICE. **The Incidence of Poliomyelitis Virus in Normal Children under 5 Years. An Interim Report.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Oct., v. 17, 231–8, 1 fig.

This paper is an interim report of the results of a survey of the carrier rate for poliovirus in the faeces of children aged 0–4 years which is being carried out by the Public Health Laboratory Service in England and Wales. The report covers a year from April 1957. 21 laboratories fairly uniformly distributed throughout the country cooperated in the study. Almost all the children were living in towns because of the difficulties in collecting samples from country districts. Samples were collected weekly from children randomly selected from the birth registers, and approximately equal numbers of children born in each of the last 5 years were studied. Virus isolations were made in HeLa cells in all laboratories and supplemented in a few by the use of human amnion or monkey kidney cells. The incidence of poliovirus carriage rose as the number of notifications (both paralytic and non-paralytic) increased, but declined rather more slowly than the case incidence. Type 1 virus was most frequently isolated and Type 2 most rarely.

The carrier rates for the different areas could be divided into high and low areas having carrier rates over or under 12 per 1,000 specimens. In general the areas with high carrier rates had higher notification rates and were more industrialized. There were exceptions; for example, Exeter had a high notification but low carrier rate and Newcastle a low notification and a very high carrier rate (25 per 1,000 specimens). In the areas with low isolation rates no Type 2 or 3 virus was isolated.

In addition to poliovirus, Coxsackie, adenovirus and unidentified agents were recovered. The Coxsackie carriage seemed to follow that of poliovirus fairly closely, whereas adenovirus was equally prevalent in all quarters of the year except for a decline in July to September.

A. J. Beale

ZALMANZON, E. S., RAPPOPORT, R. S., ITSELIS, F. G. & TALINSKAIA, A. F. **The Problem of the Dissemination of Poliomyelitis Virus in the Environment of the Patient between Epidemics.** *Problems of Virology.* London. 1957, v. 2, Nos. 5/6, 348–53, 4 figs. [19 refs.] [Translated from Russian.]

This interesting paper concerns the spread of poliovirus to the contacts of a patient. The study was undertaken in Moscow at a time when poliomyelitis was not epidemic but when sporadic cases were occurring. In all, 45 incidents were studied, 14 in babies' crèches, 5 in kindergartens, 2 in schools and 24 in the families of the patients. The poliovirus isolation rate was highest in the young children under 3 years of age who had a 10% isolation rate. In all, 721 persons were examined and 37 polioviruses were isolated, 20 Type 1, 7 Type 2 and 10 Type 3 (these were the first Type 3 viruses to be isolated in the U.S.S.R.). In addition to poliovirus a large number of untypable

cytopathogenic agents were isolated. In all, 80 strains were isolated and the isolation rate for children under 3 years was 20·8%. The findings in 4 incidents are depicted diagrammatically. These demonstrate that the virus spreads to a high proportion of the children of a crèche when one becomes clinically infected but that spread to staff members or to members of a family is much less common. They also illustrate the high incidence among young children of untypable agents. This study was carried out with human embryonic tissues and an inoculum of 0·1 to 0·2 ml. of faecal suspension, a technique which is not of maximal sensitivity. *A. J. Beale*

PECZENIK, A. & DUTTWEILER, D. W. **A Preventable Outbreak of Poliomyelitis.** *Pub. Health.* 1958, Oct., v. 73, No. 1, 16–21, 1 fig.

2 United States Army Medical Officers describe a small outbreak of poliomyelitis among the children of U.S. troops stationed in Austria. There were 5 paralytic cases, including 1 of bulbo-spinal type, and 1 non-paralytic case. The initial patient was a mild and undiagnosed case when admitted to hospital for a tonsil and adenoids operation. 5 days after the operation her brother developed clinical signs of poliomyelitis, and it was only then discovered that the first child had a slight limp and had suffered from an acute illness with headache, sore throat, slight fever and weakness of the leg 7 days prior to admission to hospital.

The authors' thesis is that this was the time for vigorous preventive action among the child contacts, especially 14 days' quarantine and administration of gamma globulin. This was not done and the outbreak followed. The difficult subject of hospital infections is discussed, and support is given to COLEBROOK'S proposal [this *Bulletin*, 1956, v. 31, 181] for the appointment of an "infection control officer" for some hospitals at least. *H. Stanley Banks*

DICK, G. W. A. & DANE, D. S. **Vaccination against Poliomyelitis with Live Virus Vaccines. 4. A Review of the Present Position.** *Brit. Med. J.* 1958, Nov. 15, 1184–6. [19 refs.]

In this paper Professor Dick and Dr. Dane review critically the present status of attenuated poliomyelitis vaccine. The possible advantages of attenuated poliovaccine are that it can be given by mouth, it is cheaper, and it may give better immunity. Attenuated poliovaccine has been found to prevent reinfection with polioviruses, whereas formalin-killed vaccine as used at present does not prevent such alimentary reinfection either by attenuated strains or by wild polioviruses in nature. They review the problem under 5 headings.

1. *Safety to the vaccinee.* Attenuated poliovaccine has been administered to thousands of people now, without any illness being definitely attributed to it. Apart from the observations of DANE *et al.* [this *Bulletin*, 1957, v. 32, 311] the increase in virulence of a virus excreted over that administered has been slight.

2. *Safety to the community.* It is clear that when attenuated strains are administered they can spread to contacts. The virus excreted by vaccinated persons has been repeatedly found to be of slightly increased neurotropism for monkeys. Professor Dick and Dr. Dane believe that these excreted viruses are as virulent as some strains of poliovirus which are found in nature, and that it is at least possible that these strains may with repeated passage in man change to even greater virulence. The question of spread is considered to be crucial. It may be beneficial but it may also be potentially dangerous. In conducting trials of attenuated vaccines these possibilities must be borne in mind and thoroughly investigated.

3. *Effectiveness in the vaccinated person.* This has been assessed by neutralizing antibody determinations. Usually over 90% of the vaccinated persons produce an antibody response. The results of Dane *et al.* [below] show that the response of children to the TN rodent-adapted Type 2 poliovirus is very similar in titre and in rate of decline to that observed after 2 doses of formalin-killed vaccine. Whereas a third dose of formalin-killed vaccine has been shown to produce a booster effect, the result of attempting to reinfect a subject with attenuated vaccine was problematical. Immunity might be maintained in this way but it is at least possible that reinfection might prove difficult to achieve.

4. *Effectiveness to the community.* The fact that attenuated vaccines seem to prevent alimentary reinfection opens a prospect of eliminating poliovirus from the community by blocking its spread. Killed vaccine as at present used does not affect the spread of poliovirus in nature; but HOWE [this *Bulletin*, 1958, v. 33, 824] has shown that potent killed vaccine does limit alimentary infection in chimpanzees.

5. *Use and testing of current attenuated strains.* Attenuated strains could be used (a) instead of formalinized vaccines, (b) to supplement such vaccines, (c) to halt epidemics, and (d) in countries whose financial resources do not permit the use of formalinized vaccine. In the present state of knowledge it is not considered wise to use attenuated vaccines under the headings (a), (b) or (c) since insufficient is yet known about the efficacy of formalinized vaccine when a large proportion of a population are properly immunized on the one hand, and also insufficient is known about the safety of the attenuated strains to warrant their mass use. It is considered, however, that in countries whose financial resources do not permit the use of formalinized vaccine but where there is an indication for poliovaccine, a carefully controlled trial of an attenuated vaccine might be warranted. *A. J. Beale*

DANE, D. S., DICK, G. W. A., BRIGGS, Moya & NELSON, R. **Vaccination against Poliomyelitis with Live Virus Vaccines. 5. Neutralizing Antibody Levels One Year after Vaccination.** *Brit. Med. J.* 1958, Nov. 15, 1187–8, 1 chart.

One of the advantages of attenuated poliomyelitis vaccines usually canvassed is that the immunity is likely to be more durable. During the first half of 1956 a number of children in Northern Ireland were vaccinated orally with the attenuated SM Type 1 and

TN Type 2 poliovirus strains. Serum samples from 5 out of 6 adults fed with SM Type 1 virus tested a year after vaccination showed a fall in Type 1 neutralizing antibody titre. 1 had a rise in titre from 1 in 8 to 1 in 256. He also had a rise in titre of Type 2 poliovirus neutralizing antibodies and it is assumed that he had a natural poliovirus infection. In addition a second serum sample was obtained from 60 children who were vaccinated with the TN Type 2 strain a year previously. The level of neutralizing antibodies found in these 60 children was very similar to that found in previously non-immune children 1 year after a course of 2 injections of formalinized vaccine [MEDICAL RESEARCH COUNCIL, this *Bulletin*, 1957, v. 32, 510]. The results are presented graphically and it is not easy to determine the individual titres accurately. However, it appears that about one-half the children did not show a significant change of titre. Roughly equal numbers of the remainder showed 4-fold or greater rises or falls in antibody level. 6 of the children who had a rise in Type 2 antibodies had serological evidence of Type 1 or 3 poliovirus infection during the year, but it is thought that the rise in antibody titre to Type 2 virus was often due to continued multiplication of the TN virus in the alimentary canal. Attention is drawn to the fact that many children had a fall in antibody titre. *A. J. Beale*

CLARKE, Suzanne K. R., GOFFE, A. P., STUART-HARRIS, C. H. & HERZOG, E. G. **A Small-Scale Trial of Type III Attenuated Living Poliovirus Vaccine.** *Brit. Med. J.* 1958, Nov. 15, 1188–93, 3 figs. [20 refs.]

This paper is a valuable addition to our knowledge of the performance of attenuated poliovirus vaccines.

It has been found that 2 doses of formalin-killed poliovaccine do not prevent alimentary infection with polioviruses in nature or after feeding of attenuated strains. It has been suggested, therefore, that a planned exposure to alimentary infection of attenuated virus should be beneficial for individuals previously inoculated with killed vaccine, since it should boost circulating antibody and confer immunity to reinfection of the alimentary tract.

14 boys, aged 6–15, resident in a long-stay orthopaedic institution, who had been previously (about 3 months) immunized with 2 doses of British killed poliovaccine, were fed $10^{4\cdot8}$ TCD50 of the attenuated Type 3 strain obtained by SABIN (12 a_1b (KP4)) [this *Bulletin*, 1957, v. 32, 1032] in gelatin-coated capsules. The response to the killed poliovaccine was similar to that previously found for British vaccine [*ibid.*, 510; 1958, v. 33, 560]. All but 1 child showed a rise in antibodies to the Type 3 component, but only 3 of the children had been without detectable antibodies to the Type 3 component before vaccination.

Before the administration of virus the children were not excreting virus in their stools. No child showed any ill effect after ingestion of the attenuated poliovirus. Only 3 out of the 14 children showed an increase in antibody level. All 3 of these children excreted virus in their faeces for long periods, as did 2 other children. All the remaining children showed no evidence of poliovirus infection except for 1 who showed transient virus excretion. 2 factors were considered important in influencing infection, (a) age: 4 of the 5 infected children were the youngest in the group (6–7 years); there was only 1 other aged 6–7, and this child had a titre of Type 3 neutralizing antibodies of 1: 1,024 before being fed this virus; (b) antibody level: the geometric mean antibody titre before inoculation to Type 3 virus was 1: 42·2 in the infected children and 1: 351·8 in the uninfected.

A virulence test was performed on the first and last virus isolates obtained from the children. The vaccine virus did not cause any lesions after intracerebral injection of over 6 million TCD50 of virus, although Sabin [*loc. cit.*] does report that occasionally animals are paralysed after intraspinal inoculation. On the other hand, the majority of the strains isolated from the vaccinated children did produce lesions and paralysis following intracerebral inoculation of undiluted tissue culture fluid or a 1 in 100 dilution of it. In 2 instances the first isolate did not produce any lesions. The second isolate obtained from 9–31 days after administration was uniformly virulent, producing paralysis and histological evidence of poliovirus infection. The histological lesions were often severe and widespread. Despite the fact that no spread of virus to contacts was observed, the authors believe more study of the properties of attenuated viruses excreted by vaccinated individuals is required before their mass use could be advised. *A. J. Beale*

MAYER, V., with the technical assistance of G. ROMANCÍKOVEJ. Sledovanie pretrvávania vírusov Coxsackie v internátnom kolektive mládeže. [**Examination of the Persistence of Viruses belonging to the Coxsackie Group in a Group of Boarding-School Children**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 4, 235–41. [16 refs.] English summary (8 lines).

In October 1956 an outbreak of febrile illness with meningeal symptoms occurred in a girls' residential school in Bratislava. A strain of virus pathogenic for infant mice was isolated from the stools of 1 of 4 patients who were admitted to hospital, and a rise in titre of neutralizing antibody to the strain was demonstrated in paired sera from the same patient. The virus was identified as Coxsackie group A type 6, and could also be isolated from 6 of 73 stool samples taken at intervals from 20 girls who were in close contact with the 4 patients. In 1 instance the virus was isolated 108 days after the outbreak of illness.

D. J. Bauer

BENDA, R. Výsledky vyšetřování na přitomnost sérových protilátek Coxsackie (skupina B) v populaci. [**Results of an Examination of the Presence of Coxsackie Serum Antibodies (Group B) in the Population**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 6, 380–86. [64 refs.]

The English summary appended to the paper is as follows:—

"In 1957, 750 human serums were examined as for the presence of CF antibodies against Coxsackie viruses, group B (type 1—5). An average incidence was found of 4.8 p. c. Neutralizing antibodies against the mentioned types of viruses were followed in 20 elected serums and in 3 samples of normal human gamma globulin. The presence of the neutralizing antibodies in the serums is almost regular, in the gamma globulins quite regular.

"The whole of the results makes clear that all serologic types of Coxsackie viruses, group B, appeared in the population of Bohemia during last years."

MAKOWER, H., SKURSKA, Z. & HALAZINSKA, L. **On Transplacental Infection with Coxsackie Virus.** *Texas Reports on Biol. & Med.* 1958, v. 16, No. 3, 346–54. [38 refs.]

Coxsackie A4 virus was isolated from the meconium obtained on the first day of life from a child who died at the age of 4 days with multiple congenital abnormalities (the exact abnormalities are not recorded). No infectious agent was isolated by the inoculation of cerebrospinal fluid into adult mice intracerebrally or intraperitoneally. Tests for toxoplasm infection were also negative. The mother's serum inhibited Coxsackie A4 virus to a titre of 1 to 50. The authors suggest that Coxsackie A4 virus might have been the cause of the congenital abnormalities. *A. J. Beale*

SCARABICCHI, S. Le lesioni cardiache da virus Coxsackie. [**Cardiac Lesions in Coxsackie Virus Infection**] *Giorn. Di Malattie Infettive e Parassit.* 1958, Oct., v. 10, No. 10, 882–6, 2 figs. [16 refs.]

The lesions were slight and transitory.

GRESSER, I., HARDY, J. L. & SCHERER, W. F. **The Growth Curve of Japanese Encephalitis Virus in the Vector Mosquito of Japan,** *Culex tritaeniorhynchus. Japanese J. Exper. Med.* 1958, Aug., v. 28, No. 4, 243–48, 1 fig. [12 refs.]

Previous experiments [this *Bulletin*, 1959, v. 34, 30] had shown that *Culex tritaeniorhynchus* could be easily infected experimentally with Japanese encephalitis virus and could transmit it to susceptible animals. In the present experiments batches of 200–500 laboratory-reared mosquitoes were allowed to feed on an immobilized chick with viraemia following infection with a strain of virus isolated from *C. tritaeniorhynchus* and passaged 4 times in mice. The level of viraemia was estimated by titration of blood taken just before the mosquitoes were fed. 4 groups of mosquitoes were fed on chicks with log. blood titres of 2·4, 1·5, 1·2 and 0·4 from which it was estimated that the initial titre of virus in the respective groups of mosquitoes would be 12–0·15 mouse LD50 per mosquito [$10^{-1.2}$ is a misprint for $10^{-0.2}$ in the text]. With the 3 lower virus doses virus could not be detected in the mosquitoes 2–4 days after feeding (mosquitoes with the highest dose were not tested on these days). Virus could be detected in almost all of the mosquitoes receiving the 3 highest doses between the 5th and 7th days after feeding, and in all 10–12 days after feeding. Maximum titres were, in general, reached soonest after the highest dose. By 3 weeks after feeding all mosquitoes remaining in all 4 dose-groups had titres of virus about 100,000 times the initial level. *C. E. Gordon Smith*

GRESÍKOVÁ, M., with the technical assistance of A. STYKOVÁ. **Recovery of the Tick-Borne Encephalitis Virus from the Blood and Milk of Subcutaneously Infected Sheep.** *Acta Virologica.* Prague. 1958, Apr.–June, v. 2, No. 2, 113–19, 4 figs.

6 sheep were inoculated subcutaneously with the Czechoslovakian "Hypr" strain of tick-borne encephalomyelitis virus. This strain had undergone 47 mouse passages and 1 hamster passage. 4 of the sheep had no febrile reaction, 1 had fever on the 8th and 1 on the 3rd and 8th days after inoculation. No clinical signs were detected. Viraemia was detected in all for periods varying from 1 to 5 days from 24 hours to 5 days after inoculation. The milk was found to contain virus in 5 of the sheep for periods of 4–6 days from 48 hours to 7 days after inoculation. Neutralizing antibodies were found in both blood and milk 3 months after infection. Sheep milk is extensively used in the area for cheese making.

C. E. Gordon Smith

FEDOROV, I. V. **The Occurrence of Neutralizing Antibodies to the Virus of Russian Spring-Summer Encephalitis in the Blood of Wild Birds.** *Problems of Virology.* London. 1957, v. 2, Nos. 5/6, 343–45. [Translated from Russian.]

The sera were stored dried on filter paper and appear to have been tested in pools although this is not explicitly stated. 117 sera were tested from 12 species of wild birds. Neutralizing indices of 100 were considered positive and 50–100 as doubtful. Positive pools were found from the common bullfinch, the missel-thrush, the yellow-hammer, the wagtail and the nuthatch [specific names are not quoted].

C. E. Gordon Smith

DUBOV, A. V. **Clinical Peculiarities of Tick-Borne Encephalitis in the Kuznetsk Basin District among Various Population Groups.** *Problems of Virology.* London. 1957, v. 2, Nos. 5–6, 357–60. [15 refs.] [Translated from Russian.]

A study was made of 2 communities: (1) 2 mining villages in a forest zone into which there had been large scale immigration since 1945; 20% of its present population arrived in 1955 alone. (2) Villages in woodland and scrub concerned with forestry and agriculture and to which there has been no recent influx of population.

In the first community there was an outbreak of mild tick-borne encephalomyelitis in 1942 when there had not yet been an influx of population. After the war focal forms of the disease began to predominate in this community, all in persons without previous contact with the *taiga* forests. In the second community the disease

has continued to be mild. Between 1953 and 1955 only 3% of the cases in the second community were encephalitic or encephalomyelitic compared with 22% in the first community. Encephalitic forms affected mainly factory workers and housewives who were only occasional visitors to the forest. Only 1 of 60 patients in the second community had permanent sequelae compared with 27 of 65 in the first community. The authors suggest that these differences are due to some degree of immunity developed by those in frequent contact with the *taiga* forests. *C. E. Gordon Smith*

WORK, T. H. **Virological Aspects of Kyasanur Forest Disease.** *J. Indian Med. Ass.* 1958, Aug. 1, v. 31, No. 3, 111–113. [12 refs.]

The virus of Kyasanur Forest disease [this *Bulletin*, 1958, v. 33, 444] was isolated from 37 of 45 sera from 36 patients. There were only 3 failures to isolate virus from specimens obtained during the first 10 days of the disease; no isolations were made from 5 samples between the 11th and 14th days of the disease. The sera travelled 500 miles on wet ice to the laboratory before isolations were attempted. There were isolations from 4 of 8 cerebrospinal fluids obtained in the first 10 days of the disease. Virus was also isolated from heart and skeletal muscle, liver, spleen, lung and kidney, but not from brain of patients who died between the 7th and 9th days of the disease. The diagnosis was established by isolation or serology in 44 of 112 reported cases. 40 of these patients were males and 31 of them were aged 20–40 years; there were only 4 under 15 years. Virus was also isolated from 3 langur and 3 bonnet macaque monkeys at autopsy, and from more than a dozen pools of *Haemaphysalis* ticks. Man-to-man transmission has not been observed. There have been 9 laboratory infections with this virus in India and 5 in the United States. *C. E. Gordon Smith*

LAKSHMANA RAO, R. **Clinical Observations on Kyasanur Forest Disease Cases.** *J. Indian Med. Ass.* 1958, Aug. 1, v. 31, No. 3, 113–16.

The disease has a sudden onset with fever and severe frontal headache. There may be neck rigidity, and severe cramps affect especially the nape of the neck, the back and the calves. The fever of 102–104°F. is usually continuous, lasting 5–12 days or more and there may be a febrile relapse after 1–2 weeks without fever. Confusion and restlessness accompany the fever. Conjunctival injection is common in the first few days and the palate is suffused, with maculopapular haemorrhagic spots. There may be discrete tender lymphadenopathy especially in the neck in some cases. There is severe prostration. Gastro-intestinal symptoms are not uncommon. Haemorrhagic complications include bleeding gums, epistaxis, haemoptysis, haematemesis, melaena and red blood in the stools. Death preceded by coma usually occurs within 8–12 days. There is leucopenia, and albumin and casts in the urine. Treatment is symptomatic and directed mainly to maintaining fluid balance and controlling haemorrhagic tendencies. *C. E. Gordon Smith*

NARASIMHA MURTHY, D. P. **New Virus Disease—Kyasanur Forest Disease.** *J. Indian Med. Ass.* 1958, Aug. 1, v. 31, No. 3, 125–7.

The human cases of Kayasanur forest disease have occurred in part of Mysore State about 200 sq. miles in area. The affected villages are surrounded by forest in which there has been an epizootic of fatal disease in monkeys. In the first village 4 cases and 2 deaths were reported in February 1956 and by the end of April there had been 19 cases and 6 deaths; the population of the village was 73. By this time neighbouring villages had been involved but the disease subsided for the year by the end of April. 8 months later, in January 1957, monkey deaths and human cases were again reported from the same area but there were many more cases during the second outbreak [no estimate of the numbers is given]. *C. E. Gordon Smith*

SIDHU, A. S. & TANEJA, P. N. **Encephalitis Epidemic in Infants and Children in Delhi (1954–55): (I) A Three Years Follow Up Study.** *Indian J. Child Health.* 1958, Sept., v. 7, No. 9, 589–607, 5 figs. [32 refs.]

A widespread epidemic of encephalitis with a case fatality rate approximating 50% occurred in northern India in the late summer of 1954; clinical and epidemiological accounts of it were given at the time [this *Bulletin*, 1956, v. 31, 117; 1957, v. 32, 124 *bis*]. Among the cases occurring in children in New Delhi, 109 survivors have now been followed up for 3 years. No less than one-third of these cases at the time of discharge had residual neurological complications, and in considerably more than half of this group the residua persist after 3 years and 11% of them died during the period. On the other hand, apparently complete recovery was noted in 41·6% of them within 2 months of their discharge. The neurological residua were classified mainly in 3 almost equal numerical groups: (1) upper motor neuron paralysis, (2) objective mental retardation, and (3) Parkinsonian syndrome; 4 patients had severe progressive Parkinsonism. Evidence of cortical atrophy was found by pneumoencephalography in 11 out of 12 patients examined. The exact incidence of post-encephalitic Parkinsonism resulting from this outbreak cannot be determined for many years. Meanwhile the present incidence (11% of survivors) after this outbreak is compared in a table with the recorded incidence after encephalitis lethargica (some 20–40%), Japanese B encephalitis (seldom observed) and St. Louis encephalitis (11%). *H. Stanley Banks*

TESCHNER, D. Die Dipterenfauna an menschlichen Fäkalien. Ein Beitrag zur hygienischen Entomologie. [**Flies and Human Faeces. A Contribution to Hygienic Entomology**] *Ztschr. f. Angewandte Zool.* 1958, v. 45, No. 2, 153–99, 3 figs. & 6 charts. [45 refs.]

In the literature on studies of the insect fauna which visit human excrement the results have differed considerably in different countries. For example studies

in North America indicated that *Musca domestica* was the most important vector for transmitting disease agents from faeces to man, but different results were obtained in studies in other parts of the world. This paper contains a detailed account of a study of the Diptera caught by means of traps baited with human faeces and by insect-nets in a suburb of Brunswick. The methods of investigation, together with the type of trap which was used, are described. Many pages of description and numerous tables cover the wealth of information obtained in the entomological investigation of the catch. The tables give numerical details of flies caught week by week and their identification. There is a long discussion of the findings from the biological and hygienic points of view.

It was found that of the Diptera which were caught "the genus *Paregle* Schnabl" was the most prevalent. In the summary (in English) a list is given of a number of these Diptera which are "the most significant carriers of infections from human excrement to men". A striking point is the rarity of *Musca domestica* which was not found in the first experiments. In another experiment 880 marked house flies were released and only 2 of these were trapped. It is also pointed out that "the hygienic importance of one and the same Diptera-species can be different in diverse climates. So, in the zone of the present tests, the species *Musca domestica* L. is out of the question for infections which suppose an alternate visit of human faeces and food".

M. E. Delafield

STOPPANI, A. Andamento delle infezioni tifoparatifiche nella Provincia di Perugia negli ultimi 17 anni. [**The Incidence of Typhoid and Paratyphoid in Perugia Province in the Last 17 Years**] *Giorn. di Malattie Infettive e Parassit.* 1958, Oct., v. 10, No. 10, 914–23, 3 figs.

Perugia province is in the Umbria region, and the period covered in this paper is from 1939 to 1955. In all, 6,906 cases of typhoid and 1,737 of paratyphoid were notified to the appropriate authorities, among an average annual population of 600,000. The curves of incidence resemble those for Italy as a whole, but the years 1939–44 showed a gradually increasing incidence, reaching the peak in 1944. [This has been mentioned as the year of maximal incidence in a number of reports from Italy (this *Bulletin*, 1958, v. 33, 105, 935).]

There is a marked seasonal incidence with an August peak. Death rates and case fatality rates have shown a steady fall (with some fluctuations) over the years, with a specially rapid decline from 1950 coinciding with extended antibiotic treatment.

5 localized epidemics are described which occurred in 1944, 1947, 1950 and 1955 in areas outside the capital, and in 1952 in Perugia itself. In 1 instance ice contaminated by sewage was regarded as the infecting agent and 90 cases occurred in 2 months in a population of only 2,100. In the 1955 outbreak typhoid and salmonellosis due to *Salmonella typhimurium* were caused through eating raw vegetables contaminated with sewage. The largest outbreak occurred in Perugia itself in a sweet factory, where owing to a deficient supply of drinking water, the operatives drank nonpotable water intended for industrial purposes. 154 cases of typhoid, 74 of paratyphoid B and 1 of paratyphoid A were found [the total number of workers is not given]. It was ascertained that many had avoided taking their TAB vaccine [compulsory in Italy for food-handlers]. All the hospitalized patients were treated with chloramphenicol, and although there were a number of relapses only 1 patient, who also had a cardiac condition, died.

Stoppani remarks that these local epidemics were really a good thing in the end as they stimulated the respective local sanitary authorities to improve, repair and extend water supplies and sewerage, and also to supervise more closely the handlers and the handling of food at all stages.

[Compared with the text the figures in Table 1 of the total annual number of cases of the 2 diseases seem to have been transposed.] *W. K. Dunscombe*

NEILL, W. A., MARTIN, J. D., BELDEN, E. A. & TROTTER, W. Y. **A Widespread Epidemic of Typhoid Fever traced to a Common Exposure.** *New England J. of Med.* 1958, Oct. 2, v. 259, No. 14, 667–72, 4 figs. [11 refs.]

This outbreak consisted of 34 cases of typhoid fever, widely disseminated over 8 States, and all resulting from a common exposure to sewage-contaminated drinking water at a religious conference during August in Missouri. The sewage system of the camp site had been completed only a few days before the campers began to arrive. The toilets and septic tank were situated 160 feet uphill from the well used as drinking water in the camp. During the meeting this well water became visibly contaminated, and its use was discontinued after a few days. Nevertheless, among 373 participants in the meeting who were followed up, 209 had a short diarrhoeal illness 1–4 days after arrival, 35 had a similar diarrhoeal illness about 10 days after arrival, and 34 had typhoid infection. No aetiological agents of the two diarrhoeal illnesses were discovered. Among 21 cases of proved typhoid infection, 16 clinical cases, 1 subclinical or asymptomatic case in a child, and 1 carrier were infected with phage type C-2, 1 with phage type N, 1 with phage type C-1 and 1 with a W form. The carrier was probably the original source of the C-2 infections. The remainder of the typhoid cases though not bacteriologically proved, were confidently diagnosed as typhoid fever on clinical grounds.

This is alleged to be the first typhoid epidemic of some size in which the patients were traced by phage typing to the carrier who infected them.

H. Stanley Banks

ROBERTS, D. W. T. & BARRON, S. L. **Typhoid Fever with Vulvovaginitis.** *Lancet.* 1958, Nov. 15, 1043–4, 1 fig. [17 refs.]

Mucosal ulcers, particularly of the mouth and female genitals, are well recognized in typhoid fever, although little has been heard of them in Britain for many years.

2 cases of genital ulceration are reported, in girls recently returned from the Continent, and in both the genital condition preceded the diarrhoea and main symptoms of typhoid fever.

The first patient, a girl of 15, had vulvitis with shallow ulcers of the labia minora covered with seropurulent exudate and a yellowish membrane, from which *Salmonella typhi* was cultured. The soreness of the vulva appeared 2 days after the onset of the headache and fever which proved to be the first symptoms of typhoid fever. She was treated with chloramphenicol and the ulcers healed in 2 weeks. The second patient, aged 21, had acute vaginitis with leucorrhoea, and also probably salpingitis. A vaginal swab showed *Trichomonas vaginalis*, but no salmonellae were cultured from this region, although *Salm. typhi* was grown from the blood and faeces. She also responded well to chloramphenicol treatment, and, although she had a relapse of her typhoid fever there was no further vaginal discharge.

It is pointed out that this condition, which has been known as ulcus acutum vulvae, has usually a relation to some general illness, with typhoid fever high on the list. In the typhoid ulcers the most likely mode of infection appears to be by embolism, as in the characteristic rose spots of the disease.

H. Stanley Banks

RUIZ SÁNCHEZ, F., RUIZ SÁNCHEZ, A., EVANGELISTA DE HUERTA, Dolores & NARANJO GRANDA, Elba. **The Use of Phenylbutazone and Chloramphenicol in the Treatment of Typhoid Fever.** *Antibiotic Med.* New York. 1958, Nov., v. 5, No. 11, 649–59, 3 figs. [21 refs.]

Bearing in mind the beneficial effect of cortisone and corticotrophin on the fever and toxaemia of patients suffering from typhoid fever under treatment with chloramphenicol [this *Bulletin*, 1951, v. 26, 585, 586], the authors decided to test the efficiency of another antipyretic and anti-inflammatory drug, phenylbutazone, as a substitute for the above. They conducted also a second experiment in which 5 further patients suffering from the same disease were treated with phenylbutazone alone. Though the 2 series of patients were roughly comparable as regards age distribution and severity, treatment was initiated between the 7–12th day of the disease in the first series but not until 13–24th day in the second group.

Clinical impressions only could be gathered in this study: they may thus be summarized:—

(i) Phenylbutazone, at a dosage of 300–1,200 mgm. daily either by the intramuscular or oral route, combined with chloramphenicol, appeared to control the pyrexia within 24 hours, whereas previous experience had shown that on chloramphenicol alone 48 hours usually elapsed before the fever abated by rapid lysis.

(ii) Phenylbutazone alone may in some cases lead to a fall in temperature, even to normal, though bacteraemia persists: it exerts no other effect on the course of the disease.

[The design of this clinical experiment leaves much to be desired and little information of value can be gleaned from it.] *J. H. Walters*

HUDSON, J. H. **Sonne Dysentery in Dartford Borough and Rural District, 1956.** *Med. Officer.* 1958, Nov. 21, v. 100, No. 21, 323–4.

In 1956 when England and Wales experienced "an all time record incidence" of dysentery, Dartford had its share of this dysentery. The events in Dartford are described; dysentery appeared in January when 8 cases were notified from a mental deficiency hospital. In the succeeding months a few cases appeared in most weeks, but in the fourth week of June there was an explosive rise to 43 cases notified by doctors and teachers, followed by weekly numbers of 33, 24, 12 and 14. Then the outbreak died down. Most of the infections were in 2 schools and of a total of 221 cases recorded in a table 1 school area had 24 cases, another school area had 136 and 61 were notified elsewhere. A survey of families with patients or contacts was carried out with bacteriological examination of some 1,600 faecal specimens. Some of the experiences and problems of the survey are described.

Some impressions gathered in the course of the experience are: (1) doctors and teachers were meticulous in sending in notifications, (2) about 30% of patients and contacts were positive to *Shigella sonnei* and about 2% for salmonella organisms, (3) treatment was not always effective in clearing the infection, (4) where 1 infection occurs in a household there is something like a 70% chance that some other member of the household is also infected, and (5) the "essence of control in day schools is emphasis on hand cleanliness and the exclusion of children while they have symptoms of the disease". *M. E. Delafield*

REALMUTO, A. Shigellosi a Palermo: osservazioni etio-epidemiologiche. [**Shigellosis in Palermo**] *Giorn. di Malattie Infettive e Parassit.* 1958, Oct., v. 10, No. 10, 911–14.

This is a report of an investigation into the causes of diarrhoea among the children of the poorer quarters of Palermo, in 1952–3, where a total of 215 cases of diarrhoea were investigated bacteriologically; practically three-quarters of the children were under 1 year old. 26 patients, mostly under 1 year, harboured shigellae and 25 enteritis-producing *Escherichia coli*. No salmonellae were found. The *Shigella* patients all had enterocolitis; most of the cases were due to *Sh. flexneri*, but there was no definite seasonal incidence.

The families of all the patients under 2 years of age were then examined to try to trace the source of infection. The faeces of 99 persons from 19 families were examined and organisms were isolated from 9 families; in each case the strain isolated belonged to the same biochemical and serological type as the patient's strain.

52 *Shigella* strains from a total of 314 patients and their families were then typed, 47 as *Sh. flexneri*, 4 as *Sh. sonnei* and 1 as *Sh. dysenteriae* 2 (Schmitz). *Sh. flexneri* types 1 and 2 predominated, but a few belonging to types 4 and 5 were also found; these had rarely or never been noted in the area before. A positive phenylproprionic acid test was especially valuable in determining types 1 and 2.

The author blames the low level of general hygiene for the wide distribution of infection and emphasizes the high proportion of *Sh. flexneri* where a number of persons were found with inapparent infections. The babies probably contracted the disease from their mothers or other excreters in the family and developed diarrhoea because, in contrast with the older persons they had not developed immunity.

W. K. Dunscombe

KRATOCHVÍL, J. & TARABCÁK, M. Vodný faktor v epidemiologii dyzenterie. [**The Water Factor in the Epidemiology of Dysentery**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 4, 271–5, 1 fig. & 3 graphs. [12 refs.] English summary (9 lines).

In 1955 an epidemic of dysentery occurred in 3 population groups living in temporary housing in a camp at Košice, Czechoslovakia, with an incidence of 43·8%, 50·6% and 47% in the 3 groups respectively. *Shigella flexneri* 2 was isolated from the stools of patients and from the water of a well which supplied the camp. In a laboratory investigation of the persistence of dysentery bacilli in water *Sh. flexneri* and *Sh. boydii* survived for 52 days and *Sh. sonnei* for up to 105 days at room temperature. *D. J. Bauer*

LIE KIAN JOE, SAHAB, K. & POEY SENG HIN. *Escherichia coli* **Type O111:B4 and Type O55:B5 in Djakarta, Indonesia. (Epidemiological Aspects.)** *J. Trop. Pediatrics.* London. 1958, June, v. 4, No. 1, 20–27, 2 figs.

This report gives the epidemiological features of infant gastro-enteritis in Djakarta, Indonesia— the bacteriology of these cases is described by SAHAB and JOE [see below]. The occurrence and movements of infants in 4 paediatric departments were followed; it was concluded that *E. coli* O111 B4 H2 was an important cause of infant gastro-enteritis in the area under examination, and that *E. coli* O55 B5 may also be pathogenic. Further, the O111 strains tended to become endemic, but the O55 strains did not appear to be able to flourish under the same conditions. [The original paper should be consulted in order to appreciate the exact movements etc. of the infants concerned.]

John S. Stevenson

SAHAB, K. & LIE KIAN JOE. **The Occurrence of** *Escherichia coli* **Type O111: B4 and Type O55: B5 in Djakarta, Indonesia.** *J. Trop. Pediatrics.* London. 1958, June, v. 4, No. 1, 28–33. [16 refs.]

This paper is a report of the bacteriological findings in cases of infant gastro-enteritis in Djakarta, Indonesia, during the period December 1954 to May 1957. Over 400 patients were investigated, mostly under 3 years of age; about 10% of the cases were due to *Shigella* infections, and enteropathogenic *E. coli* strains were found in about 12%—only 2 O-group *E. coli* antisera were employed, O111 and O55. The findings were as follows: 52 strains of *E. coli* O111 B4 H2 were isolated, all of which were motile, with 1 anaerogenic strain and 1 strain with an unidentified H antigen. Unlike the usual European strains, dulcite was not fermented. 7 non-motile strains of *E. coli* O55 B5 were isolated, all of which showed irregular fermentation of adonitol —this fermentation is unusual with most O55 B5 strains. *John S. Stevenson*

KEAN, B. H. & WATERS, S. **The Diarrhea of Travelers. I. Incidence in Travelers returning to the United States from Mexico.** *Arch. Indust. Health.* Chicago. 1958, Aug., v. 18, No. 2, 148–50.

Although many travellers are afflicted with diarrhoea when they go abroad, little precise information on the subject is available. The cause is not known nor can it be stated whether 1 disease or several are responsible for the symptoms. In this paper there is a report on data of incidence of diarrhoea obtained from 1,265 United States residents arriving by air at Los Angeles from Mexico and in addition from 210 tourists returning from Hawaii. On arrival these travellers were interviewed to explain the nature of the study which was being carried out and to request them to fill in a questionnaire. Among the results obtained which are fully stated and discussed are: (1) of those who had spent 7 days or more in Mexico, 326 (33%) reported that they had had 1 or more attacks of diarrhoea; (2) the sexes were about equally affected; (3) of 334 tourists who reported diarrhoea, 211 (63%) became ill during the first week in Mexico, 106 (32%) within the second week, 14 (4%) during the third and fourth week and 3 (1%) after 5 weeks. The median length of the trip for the 1,265 tourists was 11 days; (4) the incidence was highest in those under 24 years of age and decreased progressively in the older age-groups; (5) of the 1,265 tourists 83 (6·5%) reported an illness other than diarrhoea; and (6) only 7·6% of the visitors to Hawaii who spent 7 days or longer there reported diarrhoea.

" Investigations dealing with etiology and prophylaxis are in progress and will be reported separately."

M. E. Delafield

TUBERCULOSIS

SOLTYS, M. A. **Public Health Aspect of Tuberculosis in Domestic Animals.** *Brit. Med. J.* 1958, Nov. 8, 1133–6. [26 refs.]

The proper study of tuberculosis among domestic animals began in the 18th century at the time of the industrial revolution. There was a great increase at that time of the disease both in man and animals, particularly in overcrowded towns. However, it was not until 1910 that the exact relationship of the human, bovine and avian types of infection, and the transmission from one species to another, were fully understood.

Tuberculosis in cattle usually occurs as a localized disease of a chronic and slowly progressive type. It is nearly always caused by the bovine strain of the tubercle bacillus; human and avian strains having been

found only rarely in naturally infected cattle. In 1957, 73% of the total cattle in Great Britain were tuberculin-negative [and it is expected that the whole country will be an eradication area by October 1960].

Sheep are just as susceptible to bovine infection as cattle but tuberculosis is very rare among them—probably because they are never housed. Most of the tuberculosis in them is due to the avian bacillus. Information about the disease in goats is scanty, but with rare exceptions tubercle bacilli recovered from goats have been of the bovine type.

Pigs are susceptible to all 3 types of the tubercle bacillus but disease due to the human strain is rare. It may, however, occur in pigs kept on the farms attached to sanatoria but rarely causes more than localized tuberculous adenitis. The bovine strain can produce severer and more extensive disease than either of the others. The incidence of tuberculosis in pigs varies from 10 to 15%.

Tuberculosis in horses is usually due to the bovine strain of the bacillus but it may also be caused by the human and avian strains. The disease tends to be very chronic and to resemble sarcoidosis in man. The tuberculin test is less reliable in horses than in cattle or pigs.

Dogs are relatively rarely affected by tuberculosis, and in cases which occur it is believed that the human strain of the bacillus is responsible for 70% and the bovine strain for the remainder. The dog often acquires the infection from a tuberculous person in the household or in restaurants or workshops. The tuberculin test is of little value in diagnosis as the animal displays only a low degree of sensitivity.

Cats resist the human and avian strains strongly but are susceptible to the bovine strain. The incidence of tuberculosis in them is between 3 and 13%. Their main source of infection is the milk of tuberculous cows.

Practically all species of domesticated and wild birds are susceptible to the avian bacillus, to which man is highly resistant. Parrots and canaries have been infected by the human strain.

The transmission of infection by milk is controlled by pasteurization. That danger is still present (before heat treatment) is shown by the fact that in 1957, 72 of 570 milk samples examined in Cambridge [England] contained tubercle bacilli. In this connexion it is mentioned that a man suffering from tuberculosis due to a bovine strain may infect cattle.

Poor standards of sanitation in abattoirs and in the handling of tuberculous animals cause considerable risk for those working there. Dogs and cats are also a great risk in the dissemination of tuberculosis. Further public health control in these matters is required [see also this *Bulletin*, 1957, v. 32, 1140].

H. G. Calwell

LE MELLETIER, J. Enquête sur la tuberculose en milieu rural. [**Tuberculosis in Rural France**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, Sept., v. 6, No. 6, 606–22.

This investigation was undertaken throughout metropolitan France in order to ascertain the facts about the incidence of tuberculosis in rural areas, to discover its causes and to suggest remedial measures.

The rural population is taken to comprise all communities of not more than 2,000. It accounts for about one-half of the total population of France [42·7 million (1954 census)]. The basic industry is agriculture but there are great diversities in the people and their ways of life. Seasonal workers are a feature of the rural areas and they are in a particularly unfavourable position. In the neighbourhood of the larger towns, however, there is little difference between town and country dwellers.

Tuberculin surveys, details of some of which are given, show that while the reactor rate has been falling in the towns, it has risen in the country. The information available is fragmentary. Morbidity returns are also fragmentary as there is no uniformity of notification. It is the impression that the proportion of tuberculous patients with advanced and serious disease is very high among agricultural workers compared with industrial workers (for example 33% against 18%).

Formerly the tuberculosis death rate was lower in the country than in towns but this is no longer so, and the present rural rate corresponds to the rate for the whole of France and in some regions is rising.

The spread of infection is favoured by bad housing, by the movement of seasonal workers and by failure to discover infectors. Although bovine tuberculosis is common in milk cows in France (reactor rates 20–60%), human disease of bovine origin is thought to be rare and there is no strong evidence to the contrary. Nevertheless, eradication of tuberculosis in cattle is an essential part of the programme to control human tuberculosis.

The standard of housing in the rural areas is very low, and although food is generally sufficient in quantity it is often of inferior quality; for example, fresh vegetables and fruit are scarce. Alcoholism is widespread and more than one-half of the rural patients admitted to sanatoria with tuberculosis are chronic alcoholics. In addition the rapidity with which the traditional way of life is being changed plays a part in the aetiology of tuberculosis in the country.

The fight against tuberculosis is waged with difficulty because of the great area to be covered, the comparative poverty of the country as opposed to the town, the small heed the countrymen pay to illness unaccompanied by definite symptoms, the habit of some doctors of treating the patient at home rather than sending him to a sanatorium, in order to get fees, the lack of health education, the lack of suitable dispensary and X-ray facilities and finally poor coordination between the various branches of medical work.

Le Melletier suggests that the general standard of hygiene should be improved by the provision of better housing, by health education and by a campaign against alcoholism. Social insurance schemes should be extended to the country. There should be more and better equipped tuberculosis dispensaries and mass radiography should be extended. Bovine tuberculosis should be controlled and there should be better coordination of services with, at least, notification of all cases of tuberculosis to the dispensaries. *H. G. Calwell*

YOSHIOKA, H., MOROOKA, T. & KURATA, M. **Tendency of the Tuberculosis Mortality in Post-War Japan Before and After 1950.** *Yokohama Med. Bull.* 1958, Aug. v. 9, No. 4, 225–42, 4 figs. [29 refs.]

This study of tuberculosis mortality rates in Japan since 1947 is based on crude, sex and age-specific and corrected death rates.

The crude death rate from tuberculosis fell from 187·2 per 100,000 in 1947 to 62·3 in 1954. The disparity between the sexes by which the rate in males has exceeded that in females since 1932 has become wider so that in 1953 the rates were 75·5 and 59·3 respectively. The decline in the death rate was not even throughout the country.

In 1899 there was a peak of mortality at 20–24 years in both sexes (about 250), and another peak of over 200 was found in men aged 50–59 but there was no second peak in women. The high death rate in the younger age-group continued and it was 450–500 at 20–24 years in both sexes in 1935 while the peak in the older men was declining. In 1943, however, the rate was over 800 at 20–24 years in males and it was rising in older men.

No data are available for 1944–6, but in 1947 it was found that the death rate at 15–19 years had fallen to 46% of the 1943 rate for males and 54% for women; at 20–24 years it had fallen to 57 and 81% respectively. The peak had moved from 20–24 to 25–29 years, and there has been a fall every year since. The peak in the older group has remained almost unchanged. This trend is similar to that in the "civilized countries where the tuberculosis mortality is low".

Examination of corrected death rates by prefectures was made, taking the 1950 figures and the 1930 population as the standard. The highest rate was 210·4 and the lowest 88·1; the rate for the whole country was 145·2. There was evidence that as the tuberculosis epidemic waned in the cities it waxed in the rural areas. *H. G. Calwell*

EDWARDS, Lydia B. & PALMER, C. E. **Epidemiologic Studies of Tuberculin Sensitivity. I. Preliminary Results with Purified Protein Derivatives prepared from Atypical Acid-Fast Organisms.** *Amer. J. Hyg.* 1958, Sept., v. 68, No. 2, 213–31, 8 figs. [58 refs.]

This paper continues the authors' epidemiological study on the specificity of skin sensitivity to tuberculin. Previous work had led them to conclude that infection with pathogenic tubercle bacilli is not the only cause of naturally acquired tuberculin sensitivity in man. Although the cause of naturally acquired non-specific sensitivity is still unknown, they postulate that it must be a mycobacterium or closely related organism which can infect but is rarely pathogenic for man. An example of such an organism is BCG.

Antigens are available from a number of atypical acid-fast organisms, and trials are now reported in which 2 of these new antigens have been compared with mammalian tuberculin in patients infected with typical mammalian tubercle bacilli and patients harbouring the type of atypical organisms from which the new antigens were made. Tests were also made in healthy population groups in the U.S.A.

An antigen was prepared from each of 2 strains of the "Yellow" bacillus of POLLAK and BUHLER [this *Bulletin*, 1955, v. 30, 544] isolated from patients with disease resembling tuberculosis. Antigens were also prepared from 2 strains of the atypical acid-fast organism described by CROW *et al.* [*ibid.*, 1957, v. 32, 659] as the Battey organism [from the name of a hospital in U.S.A.]. These tuberculins were known respectively as PPD-Y and PPD-B; the other tuberculin used was PPD-S (international standard mammalian tuberculin). It was decided to use a dose of 0·0001 mgm. of protein content by weight corresponding to 5 TU of PPD-S.

Mantoux tests with PPD-S and PPD-B were done on 173 hospital patients of whom 145 had yielded typical human tubercle bacilli and 28 only the Battey organism. Almost all patients infected with the tubercle bacillus had a definite fairly strong reaction to PPD-S and a smaller or no reaction to PPD-B. Patients infected with the Battey organism had larger reactions to PPD-B than to PPD-S.

134 patients in another hospital were tested with PPD-S and PPD-Y of whom 103 had yielded typical tubercle bacilli and 31 a bacillus identical with the Yellow bacillus. The sensitivity produced by these 2 organisms was found to be too similar to be distinguishable by comparative testing.

Testing of normal healthy groups of the population was done in connexion with the routine skin testing of naval recruits. The material available, limited to white recruits aged 17–21 years, consisted of tests with PPD-S for 12,037 men of whom 2,546 were also tested with PPD-Y and 9,491 with PPD-B. The reactor rates were 7·3%, 11·5% and 38·7% respectively. The results were analysed geographically for those tested with PPD-S and PPD-B; the others were too few in number for analysis. The reactor rate to PPD-S increased from North to South (6–9%) as did that to PPD-B (30–65%).

If it is allowed that a reaction to PPD-S equal to or larger than that to PPD-B is specific for tuberculous infection and that a reaction to PPD-S smaller than that to PPD-B is non-specific for tuberculous infection, it can be concluded that geographical variation in the frequency of small reactions to PPD-S can be accounted for by variations in the proportion of non-specific reactors in any group. When such reactions are excluded the frequency distributions of reactions to PPD-S for recruits from different localities are very similar to one another and also to the distribution of reactions found among tuberculous patients.

The dilution of small specific reaction by non-specific reactions may inflate estimates of the prevalence of tuberculous infection by as much as 100% in some areas. "It may also account for the lower risk of developing tuberculosis associated with small as compared with large reactions to the 5 TU test, as well as for the unusually high and unrealistic conversion and reversion rates reported from some geographic areas." *H. G. Calwell*

OMLAND, T. **Tuberculin Allergy in a Group of Geriatric Patients.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, No. 1, 51–61, 4 figs.

Omland has studied tuberculin sensitivity in a group of hospital patients aged 60–89 years, none of whom were known to have tuberculosis although there was evidence that 2 men and 4 women had suffered from the disease a long time ago. The group numbered 51 men and 92 women.

2 tuberculin tests were used simultaneously, *viz.* the Mantoux with 5 TU of PPD and the von Pirquet with adrenalinized synthetic medium tuberculin. Both tests were read at 48 hours and the diameter of induration present recorded. Right and left arms were used alternately for each test.

The known tuberculosis situation in Norway in the patients' earlier days supported the conclusion that all old persons must have been infected by the tubercle bacillus at some time but only 62% of this group reacted to the Mantoux test (5 mm. or more of induration) and 63% to the von Pirquet test (3 mm. or more of induration). The mean indurations measured 9·1 and 5·8 mm. respectively.

If it be accepted that the patients studied represent a single group as far as previous tuberculous infection is concerned the tendency towards bimodality in the frequency distribution might suggest that there exists among old people a group which is qualitatively as well as quantitatively different in its reaction to tuberculin.

The Mantoux reactor rate in men was 75% compared with 54% in women and the mean indurations were 7·7 mm. compared with 4·7 mm. The frequency distribution was markedly bimodal in women.

The tendency towards a decrease in allergy as age increased was clearly seen in both sexes. The diameter of induration was less in women than in men in all age groups.

Comparison of the diameter of induration according to sex and general clinical condition showed that there was a somewhat lower degree of allergy in patients of both sexes who were in a poor condition. This decrease was not regarded as merely another expression of the same factors underlying the change of allergy that accompanies advancing age. [See also CAPLIN, M., SILVER, C. P. & WHEELER, W. F., this *Bulletin*, 1958, v. 33, 832.] *H. G. Calwell*

BOURLATCHENKO, M. A. **Tuberculosis Infection of the Rural Population of the Carpathian Mountains.** *Problemy Tuberkuloza.* 1958, v. 36, No. 5, 3–5. [14 refs.] [In Russian.] French summary.

The following is a translation of the author's summary:—

"In this article are given statistics of infection with tuberculosis of the population, aged 0–20 years, representative of the inhabitants of the rural region of Kosov in the Carpathian Mountains.

"11,977 persons were submitted to tuberculin tests. The average figure of general infection for the group shown above is: von Pirquet reactions 33·9%, von Pirquet + Mantoux and von Pirquet + Médovikov, 45·7%. The mean figure of infection among contacts is: von Pirquet reaction 62·5%, compared with 33·9% for general infection.

"For the age group 15–17 years, the level of general infection with tuberculosis reached 50%, while contact children attained this figure at ages 3–6 years.

"The author deduces that over 60% of the non-infected population and 40% of the non-infected contacts in the rural population of the Carpathians should undergo vaccination and revaccination."

A. H. Phipps

VESSELKINA, T. A. **Tuberculous Infection among Medical Personnel in Antituberculosis Clinics in Moscow.** *Problemy Tuberkuloza.* 1958, v. 36, No. 5, 8–13. [In Russian.] French summary.

The following is a translation of the author's summary:—

"To obtain a true picture of the frequency of tuberculous infections among medical personnel, the examination of 1,946 workers in antituberculosis clinics in Moscow was undertaken in 1955. On entry into the service, 1,150 of these persons were in good health in so far as tuberculosis was concerned.

"Diminution in general infection of the medical staff of antituberculosis establishments has been noted. In the course of professional contact of 7½ years' average duration, 81 persons contracted the disease—7% of the number entering the service in good health. In the various groups, the numbers of infections were as follows: among doctors, 11·9%; for middle grade staff, 9·3%; and in the subordinate group, 5·2%."

A. H. Phipps

POPE, A. S. & GORDON, J. E. **The Impact of Tuberculosis on Human Populations.** *Amer. J. Med. Sci.* 1955, Sept., v. 230, No. 3, 317–53, 10 figs. [68 refs.]

HEYMANSON, F. E. & ELPHICK, H. R. **Accidental Inoculation Tuberculosis.** *Med. J. Australia.* 1958, Jan. 25, v. 1, No. 4, 112–13.

The subject of this accident was a laboratory technician whose tuberculin test was known to be positive. He dropped a hypodermic syringe and needle containing a suspension of tubercle bacilli and the needle caught in the leg of his trousers. He was not aware that it pierced the skin, but some days later a swelling appeared there which eventually was shown to be tuberculous, and which broke down to a shallow undermined ulcer. There was no glandular involvement, and the condition cleared after a course of chemotherapy.

This is a typical example of re-infection tuberculosis of the skin. *Charles Wilcocks*

BELOTTE, J. A propos de quelques aspects radiologiques intrathoraciques de la primo-infection tuberculeuse chez le jeune Africain. [**Radiological Aspects of Primary Pulmonary Tuberculosis in African Children**] *Méd. Trop.* Marseilles. 1958, v. 18, No 4, 670–76, 6 figs.

This radiological study of primary pulmonary tuberculosis in African children was made in an unnamed French colonial territory. The aim of the author was not to report new facts about the disease but to demonstrate some particular characteristics exhibited by it in African practice.

Adenopathy with and without visible parenchymal disease is seen as elsewhere, but Belotte believes that cavitation of the primary focus is less rare in African children than has been described in the classical accounts of the disease [in Europe]. It is difficult to be sure that the cavitation is definitely primary, unless the child has been under observation throughout the development of the condition.

Pleural reaction is frequently seen; it is usually localized. Belotte has seen several cases where extensive mediastinal fibrosis followed and persisted. This is emphasized as an example of the unusual behaviour of the disease in the African child.

Belotte does not believe that these peculiar reactions to primary tuberculous infection are due to racial factors but rather to a constitutional predisposition combined with environmental factors peculiar to the country. [If all African children in the territory have this "constitutional predisposition" it must be racial; if only some have it it may be familial or environmental.]

H. G. Calwell

Böhlau, V., Dennhardt, H. & Rothe, H. Energetische Stoffwechseluntersuchungen bei Lungentuberkulose. Der Grundumsatz vor und im Verlauf der Chemotherapie der Lungentuberkulose [**Metabolism in Pulmonary Tuberculosis—the Basal Metabolic Rate before and after Treatment**] *Ztschr. f. ärztl. Fortbildung.* 1958, Oct. 15, v. 52, No. 20, 852–5.

This paper begins with a review of previous work on the subject from 1892 onwards. It was the conclusion of the writers quoted that a raised metabolic rate in patients with pulmonary tuberculosis indicates activity of the disease and those with a normal or only slightly raised rate are likely to pursue a favourable course.

The authors estimated the basal metabolic rate in 262 patients with untreated pulmonary tuberculosis. Details of the method used are given. The rate was within the normal range in 63%, it was high in 24% and low in 13%. The type of disease present (exudative or productive) did not appear to influence the rate. The highest proportion of normal rates was found in afebrile patients, 81·7% compared with 45·2% and 55·3% respectively in febrile and subfebrile patients.

The rate was estimated on at least 3 occasions in 182 patients receiving chemotherapy. It was found to have fallen in 41·2%, to have risen in 8·8%, to be the same in 38·6% and to vary (rise and fall) in 11·5%.

The authors claim that this group of patients is the largest to have been studied in this way. They conclude that in spite of the rule that the basal metabolic rate rises with temperature, the relatively high percentage of febrile patients with a low metabolic rate in the series shows that the rule is not universally applicable in pulmonary tuberculosis. The influence of chemotherapy was such that the rate fell in almost one-half of the patients treated. *H. G. Calwell*

Nicol, V. S. & Fawns, H. T. **Observations on the Bromide Partition Test in the Diagnosis of Non-Purulent Meningitis.** *Arch. Dis. in Childhood.* 1958, Oct., v. 33, No. 171, 440–44, 2 figs.

Tuberculous meningitis may be difficult to diagnose in the earliest stages by clinical methods, but the authors found the bromide partition test described by Taylor *et al.* [this *Bulletin,* 1954, v. 29, (593); *Lancet,* 1954, v. 1, 700] a useful aid to the diagnosis of 6 cases of tuberculous meningitis and 20 of non-tuberculous meningitis.

Normally, after oral or intravenous injection of sodium bromide the ratio between the quantity of bromide in serum and cerebrospinal fluid is above 1·65. In cases of tuberculous meningitis the integrity of the blood cerebrospinal fluid barrier is affected and there is an early fall in the ratio below 1·65 towards unity, with a return to normal when the infection is brought under control. A fall does not occur in other types of non-purulent meningitis; in purulent meningitis this fall may or may not occur, but owing to the different clinical course of purulent meningitis, this type of test should not be necessary.

The method used was that described by Taylor *et al.*; bromide was estimated by the method of Hunter (*Biochem. J.*, 1953, v. 55, 42). Sodium bromide was given orally 0·25–1 gm. 3 times daily for 3 days or as a single intravenous injection containing 2·8 gm. [the solution contained 8 gm. in 30 ml.]. Venous blood, 5 ml., and lumbar cerebrospinal fluid, 8 ml., are collected 24 hours after intravenous injection and 48 hours after oral administration for bromide estimation. The authors of the original paper stress the importance of collecting lumbar cerebrospinal fluid as fluid obtained by cisternal or ventricular puncture yields different values. For each estimation 1·0 ml. of serum or cerebrospinal fluid is required. It is essential to carry out a reagent blank with each test as there is a somewhat large and variable blank value arising from reagents which must be deducted from the serum and cerebrospinal fluid values. The accuracy of the method appeared to be satisfactory but is somewhat time-consuming for a busy clinical laboratory.

In the 6 patients with tuberculous meningitis examined the bromide ratio was depressed in all. Repeat tests were done on 3 patients during treatment and clinical improvement was accompanied by a rising ratio in each case. In the 20 patients with non-tuberculous meningitis the ratio was normal in 18, 3 of whom had positive Mantoux reactions and 1 had had BCG.

The results agreed with those of Taylor *et al.* who reported 7% of false positive results in their series.

Taken in conjunction with the clinical findings, the bromide partition test appears to be a valuable adjunct in the early diagnosis of tuberculous meningitis and may prove also to be a useful criterion for following the course of clinical improvement. *P. A. Clearkin*

KIRKALDY-WILLIS, W. H. **Bone and Joint Tuberculosis in Kenya.** *Central African J. of Med.* 1958, *Aug.*, v. 4, No. 8, 324–9, 10 figs.

In the African orthopaedic unit in Nairobi one-third of the beds are occupied by patients with bone or joint tuberculosis, and the author thinks that all of them have had a minor attack of pulmonary tuberculosis. He quotes low-grade infective arthritis, subacute or chronic osteomyelitis, brucellosis and yaws as conditions which may be confused with tuberculosis, and which should be kept in mind in differential diagnosis.

For treatment he makes the point that rest in bed can be overdone, and that it is now his practice to operate "once and for all after two to three months of rest, immobilization and chemotherapy". But the mental accord between doctor and patient is perhaps more important than anything else, and if the doctor can make the patient smile and laugh, "the battle towards recovery is almost won. Real laughter is in fact of greater importance than the most carefully planned and executed operation".

The author gives operation details for spine, hip, elbow and knee, and concludes that "This problem is undoubtedly the most fascinating of all African orthopaedic problems".

[An important paper on a subject rarely discussed.]

Charles Wilcocks

STEINBRÜCK, P. Der Einfluss der Chemotherapie auf die epidemiologische Lage der Tuberkulose in der Deutschen Demokratischen Republik. [**The Influence of Chemotherapy on the Tuberculosis Situation in the Democratic German Republic**] *Ztschr. f. ärztl. Fortbildung.* 1958, May 1, v. 52, No. 9, 371–7, 6 figs.

This paper was read at a tuberculosis conference in Moscow in 1957. The total number of patients on the tuberculosis register in the Democratic German Republic has shown little change between 1948 and 1956 although the number of new cases declined from 54 to 23 per 100,000 and the tuberculosis death rate from 104 to 23.

The decline in fresh morbidity is due chiefly to improved living standards and to more intensive application of preventive measures and only indirectly to the influence of chemotherapy on infectors. The main effect of chemotherapy is seen in the falling death rate, and the influence of isoniazid was particularly seen in the sharp fall which occurred in 1952. The waning power of chemotherapy is evidenced by the fact that whereas in 1952, 96 of every 1,000 persons with sputum-positive tuberculosis died the figures in the years 1953–6 remained almost constant, being 62, 66, 64 and 61 respectively.

The mortality rate has fallen in all districts of the Republic since 1952 but the fall has become slower and there have been occasional rises. It is hardly to be expected, the author thinks, that it can fall much below 20 per 100,000 unless other measures of control and prevention are applied.

The number of patients on the tuberculosis register shows little change. This is because of the fall in the number of deaths and of the number of patients achieving a state of quiescence or recovery.

The morbidity rate has fallen markedly in children and adolescents but that of closed pulmonary tuberculosis in patients over 25 has increased since 1949. Open tuberculosis has increased only in older patients over 65. The proportion of male patients over 45 to all male patients with tuberculosis has risen from 32 to 46% and of female patients to all female patients from 22% in 1950 to 30% in 1955. The fall in the morbidity rate in children is partly due to BCG vaccination.

It is the author's experience that younger patients respond to chemotherapy better than older patients, so that sputum conversion and closure of cavities are more frequent in them. The efficacy of a tuberculostatic drug depends on it restraining the growth of the tubercle bacillus and checking the harmful reaction between bacillus and host. Recovery and healing are the function of the body tissues themselves, which may be deficient or fail with increasing age. Deaths of patients aged 0–30 years have fallen to about one-sixth between 1938 and 1955 but the reduction in men over 60 was hardly measurable and that in women over 60 fell by only 40–50%.

The number of new cases fell from 19,074 in 1950 to 7,628 in 1956 and the proportions of open cases in the total were 60·7% and 42·5% respectively. It is therefore surprising to find that the number of cases transferred to the "open" group from other classified groups of pulmonary tuberculosis has scarcely changed since 1951.

Steinbrück expects that there will be a further decrease in morbidity in young persons and a relative or absolute increase in persons over 40. He discusses steps to meet this and recommends sanatorium treatment for 9–12 months and the continuation of chemotherapy after discharge for another year. Ambulant chemotherapy by itself should only be used where sanatoria are not available. Treatment of individual patients is however not enough. There must be improvement in living standards and health education, BCG vaccination and early discovery of cases by mass radiography must be pursued with vigour.

H. G. Calwell

DAS NEVES ALMEIDA, F. & DAS NEVES ALMEIDA, J. M. **Studies on the Pantothenates of Streptomycin and Dihydrostreptomycin. Therapeutic Action of a Mixture of Pantothenates used on Patients who had proved to be clinically resistant to Streptomycin.** *Acta Tuberculosea Scandinavica.* 1958, v. 35, Nos. 3–4, 290–308.

The authors used a mixture of equal parts of streptomycin and dihydrostreptomycin pantothenates on a group of 72 patients who are described as clinically resistant to streptomycin sulphate, *i.e.*, who were failing to progress satisfactorily on this drug. All 17 of the patients whose sputa were tested had bacilli resistant to 10 and 5 μgm./cc. respectively of streptomycin sulphate and isoniazid. The dosage varied, but most patients received 2·12 gm. of the pantothenates (equivalent to 1 gm. of streptomycin sulphate) intramuscularly in 2 doses daily in 8 cc. of water. 45

patients received the treatment for between 3 and 6 months. About 52% showed some radiological improvement, and clinical improvement was noted in a larger number, but further improvement was infrequent after 4 months. The authors claim that the pantothenates resistance is often absent in patients whose bacilli are resistant to streptomycin sulphate. Toxic effects did not commonly occur. [The rather elaborate tables are hardly justified by the relatively small number of patients concerned.] *F. H. Young*

Das Neves Almeida, F. & Das Neves Almeida, J. M. **Study of the Pantothenates of Streptomycin and Dihydrostreptomycin. Tolerance of the Pantothenates of Streptomycin and Dihydrostreptomycin in Patients Intolerant of the Sulphates.** *Acta Tuberculosea Scandinavica.* 1958, v. 35, Nos. 3–4, 309–16.

This paper reports the lack of toxic effects of a mixture containing equal parts of streptomycin and dihydrostreptomycin pantothenates. 25 patients (1 had to be abandoned), including 18 with neurological manifestations, who had developed toxic symptoms following the use of streptomycin were treated. The dosage of pantothenate mixture used was the equivalent of 1 gm. of streptomycin daily in 2 divided doses.

In a controlled experiment to verify that the toxic effects were due to streptomycin, 11 patients whose streptomycin had been suspended until symptoms had disappeared were treated again with streptomycin. All showed a reappearance of symptoms in 1–10 days. 10 other patients were treated with pantothenate mixture for 35 days. Streptomycin was then substituted until toxic manifestations arose, or for 35 days. In 4, toxic symptoms did not arise, and in the other 6 they appeared later than in the first group.

F. H. Young

Bang, H. O. & Strandgaard, E. **Continued Studies on the PAS Concentration in the Blood during Treatment with Various PAS Preparations.** *Acta Tuberculosea Scandinavica.* 1958, v. 35, Nos. 3–4, 173–96, 42 figs.

PAS in different forms was given to patients 3 times a day and the drug concentration determined in the blood at intervals from 8.0 a.m. to 8.0 p.m. Graphs of the results occupy most of the space in the paper. The most consistently satisfactory and sustained levels were obtained with 2 proprietary forms of calcium PAS. Sodium PAS, solutions of which had to be freshly prepared for each dose on account of its instability, was rapidly absorbed but too rapidly excreted. "Tebamine Leo", also described as phenyl PAS, in the form of either a powder or an "emulsion" gave very variable but generally rather low levels. [See also this *Bulletin*, 1957, v. 32, 1143.]

L. P. Garrod

Viallier, J. & Cayré, R. M. Toxicité comparée pour le lapin de l'association de l'isoniazide et du para-aminosaliyclate de soude et du sel para-amino-salicylique de l'isoniazide. [**Comparative toxicity for Rabbits of Isoniazid combined with PAS and of the PAS-Isoniazid Salt.**] *C.R. Soc. Biol.* 1958, v. 152, No. 4, 613–14.

The daily subcutaneous injection of 0·05 gm. isoniazid and 0·07 gm. PAS into 16 rabbits (2 kgm.) caused severe convulsions and death of 15 after an average of 7 injections; 1 rabbit survived 20 injections and was then killed. In contrast to these results similar injections of 0·1 gm. of the salt of PAS and isoniazid into 16 rabbits caused mild convulsions and death of only 7 rabbits before the 20th injection (average 14 injections); 9 rabbits survived 20 injections and these were then killed.

The concentration of isoniazid in the brain just before death, after the mixture of isoniazid and PAS, was 6–7 μgm. per gm., and after the PAS-isoniazid salt it was 5 μgm. per gm.; in liver the concentrations were 3–5 μgm. per gm. and 5 μgm. per gm. respectively.

S. R. M. Bushby

Prescott, B., Kauffmann, Gladys, James, W. D. & Stone, H. J. **Increase of the Tolerated Dose of Isoniazid in Mice by the Use of Certain Organic Solvents.** *Antibiotics & Chemotherapy.* New York. 1958, Sept., v. 8, No. 9, 470–75. [14 refs.]

The 8 solvents used in these investigations were 7 glycols and N,N-dimethylacetamide, and they were administered to the mice diluted with water in a volume of 0·5 ml. All these solvents showed some detoxicating effect on isoniazid, for they permitted mice to withstand 300 mgm. per kgm. dose, which is lethal when given in water only. From the acute experiments propylene glycol was selected, for as a 50% mixture it enabled 30% of the mice to withstand a 15 mgm. dose of isoniazid, *i.e.* 3 times the LD50 dose of the drug in water.

In the chronic toxicity test in which the drug was given daily, 10 mgm. in 75% propylene glycol caused the death of 30 mice in 10 days most of the animals dying between the 4th and 6th days, but when it was given every third day 9 of 24 animals were still alive after 15 days. The solvent alone caused no deaths, and 10 mgm. isoniazid in water caused the death of 20 mice within 1 day and 5 mgm. daily within 7 days. The blood concentration 1 hour after 10 mgm. was approximately 12 mgm. per 100 ml., which is about twice that observed with other isoniazid-detoxicating agents, *e.g.* amino-acids with sodium glucuronate or with glycerol.

In vitro tests showed that the presence of 3·75% propylene glycol did not affect the action of isoniazid against an avirulent strain of tubercle bacilli, and in view of the low toxicity of propylene glycol the authors recommend that it be given a clinical trial as a solvent for isoniazid. *S. R. M. Bushby*

American Trudeau Society. **The Role of BCG in the Prevention of Clinical Tuberculosis. A Statement of the Committee on Therapy** [Barclay, W. R., Chairman.] *Amer. Rev. Tuberculosis.* 1958, July, v. 78, No. 1, 145.

The level of tuberculous infection is now low in the United States, but there are still some groups of people

who are at special risk, and for them BCG is advocated:—

1. Children and others living in contact with infection.
2. Physicians, nurses, laboratory workers, hospital employees.
3. Patients and employees of prisons and mental hospitals.

The Committee remark that the protection afforded by BCG is only relative. *Charles Wilcocks*

ARAI, M. **[BCG Inoculation and Tuberculin Test. A Six Year Observation at Kego Primary School in Fukuoka City, Japan]** *Igaku Kenkyu.* Fukuoka. 1958, Aug., v. 28, No. 8, 2881–2915, 20 charts. [43 refs.] [In Japanese.] English summary.

This paper describes a 6-year vaccination programme in which over 60,000 schoolchildren aged 6–12 years were tested and vaccinated with BCG. The Mantoux test was used with 5 TU of OT from 1951 to 1954 and PPD 0·2 μgm. thereafter.

The test was read at 48 hours and classified as: positive-erythema over 10 mm., pseudopositive-erythema 5–9 mm. and negative-erythema less than 4 mm. Induration, "double erythema", blisters and necrosis were also recorded. [The reviewer does not agree that erythema by itself indicates a positive reaction to the Mantoux test. A test should be read as positive *only* if there is induration of the skin, whether erythema is present or not.] Children were excluded from vaccination if they had erythema of more than 7 mm. and later if they had erythema of more than 5 mm.

During the period May 1954 to September 1956 all children with pseudopositive reactions (erythema 5–9 mm.) were kept under observation and retested every 4 months. Conversion to positive occurred in 75%, while about 15% remained pseudopositive and 10% reverted to negative.

Consideration was given to the best interval at which to revisit a school for tuberculin testing and vaccination. The author's experience of post-vaccinal reactor rates led him to the conclusion that the best interval for maintaining a high reactor rate is 4 months. The post-vaccinal conversion rate at 2 months was 60·2%, but 4 months later 18·5% and 6 months later 36·2% had again reverted. [These figures are incontrovertible evidence of impotence of the vaccine used, or of faulty technique.]

A more potent vaccine was obtained in 1956 with the result that higher conversion rates were obtained with longer lasting sensitivity. Nevertheless Arai does not consider that yearly BCG inoculations are adequate and recommends twice yearly vaccination except for those newly entering school, or first grade children for whom he recommends inoculations every 4 months. [Schoolchildren and their parents in Japan must be much more tolerant of the ministrations of the medical profession than are their counterparts in the West.]

In 1952 when children with erythema of less than 7 mm. were vaccinated ulceration occurred in 49·4%, but when those with erythema of less than 4 mm. were vaccinated ulceration occurred in only 3·3%. [This indicates that many true reactors were being vaccinated in the earlier period and that accelerated reactions to vaccination occurred because of tuberculin sensitivity.]

There were 27 newly discovered cases of pulmonary tuberculosis in the period 1951–56 and 30 cases had occurred in the 3 years before the study began. The number requiring bed rest and treatment after 1951 was 2 and before that it was 16. There was only 1 new case in 1956—a child transferred from another school. [It is not clear how many of the children who developed tuberculosis had been vaccinated or if some were natural reactors when first tested or unvaccinated non-reactors.] Isoniazid was found to depress tuberculin sensitivity in natural convertors treated with it for 3 months. *H. G. Calwell*

VENEREAL DISEASES

LAIRD, S. M. **Figures and Fancies.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 137–52, 12 figs.

This is an article which should be of absorbing interest not only to venereologists but to all social workers and even to the general public and should therefore be studied in the original. The "fancies" are perhaps even more interesting than the "figures".

The subject essentially deals with 6,588 male patients attending 2 venereal disease clinics at Manchester between which there are many differences; of these patients, 40% had gonorrhoea, 19% non-gonococcal urethritis, 16% other para-venereal conditions (such as balanitis, various skin conditions, herpes genitalis, condylomata acuminata etc.) and 25% nothing which required treatment other than reassurance.

Syphilis is not considered at all, though it is of interest to note that not a single patient reported with early infectious syphilis (apart from 1 foreign seaman) during 1957.

Full details are set out in 12 figures and 18 tables and only a few of these can be included in an abstract. In turn are considered nationality, age, meeting place, place of exposure, type of consort, geography of exposure, day of exposure, incubation period of gonorrhoea, ratio of gonorrhoea to non-gonococcal urethritis and Reiter's syndrome. Of the patients 65% came from the United Kingdom, 9% from Eire, 12% from West Indies, 6% from West Africa and 8% from Europe and the Mediterrancan area.

Some points which stand out include the differences between patients attending the two clinics, racial differences, the later age-onset of non-gonococcal urethritis than of gonorrhoea, infection rates of married men, high incidence of open-air exposure (in spite of the bad summer of 1956), week-end peak exposure rate, the very low ratio of other venereal conditions in coloured patients, the very high ratio of white patients, especially married men, reporting with no disease and the rise in gonorrhoea in 1957. Reiter's syndrome, which proves so recalcitrant to treatment, is discussed

at considerable length and the author's suggestion that it may be related to acute rheumatic fever certainly deserves consideration.

It is suggested that the venereal disease situation is fluid rather than static, is local so far as Manchester is concerned, is largely due to prostitutes or semi-prostitutes, could largely be controlled by local (police) action and is a problem reaching far beyond the sphere of the venereologist.

[This article should stimulate *more* people to ponder *longer* over the whole subject of venereal disease control, and is one more stimulus for the implementation of at least some of the Wolfenden Committee's recommendations. Parenthetically, since most exposures occurred outdoors, one wonders whether the dismal summer of 1958 resulted in a lower incidence of venereal disease.] *T. E. Osmond*

TANAMI, Y. & YAMAMOTO, J. **The Venereal Disease Problem in Japan.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 519–29, 3 figs.

This article sets out clearly the venereal disease position in Japan and the measures taken to tackle the problem. The total *reported* cases of venereal disease fell from 402,000 in 1947 to 144,000 in 1956; the respective figures for syphilis were 148,000 and 24,000 and for gonorrhoea 212,000 and 116,000 (in round figures). Thus the fall in syphilis was much greater than that in gonorrhoea. As it is probable that only 9·6% of all cases are reported these figures should be multiplied by 10.

A 1-day survey of all patients in medical establishments on 13 June, 1955 suggested that 720,000 new cases of venereal disease occur annually.

Death rates from 1947 to 1956 per 100,000 for syphilis fell from 5·7 to 3·0 and for gonorrhoea from 0·1 to 0·0; the figures for syphilis in infants were 0·37 and 0·04. Control is carried out under the Venereal Disease Control Law of 1948; this includes (1) case finding, (2) treatment and case holding, (3) health education, (4) clinical and laboratory research.

(1) includes case reporting (compulsory), contact tracing, prenatal and premarital examination (compulsory), mass blood testing, venereal disease consultation services and compulsory examination of prostitutes. (2) includes treatment clinics, home visiting, free treatment for the indigent and compulsory treatment of prostitutes.

There are 780 health centres, each with a venereal disease clinic, 48 separate venereal disease clinics and 30 venereal disease hospitals; 150,000 cases of venereal disease were treated in these during 1956.

Case reporting and contact tracing leave much to be desired, while prostitutes are scattering among the general population and thus avoiding detection. The Ministry of Health and Welfare is responsible for the venereal disease control programme while the department of health of each prefecture carries out measures recommended; at the local level responsibility lies with the health centres.

The authors' conclusions suggest that all treatment should be free and that more workers and more money are necessary to increase the efficiency of contact tracing and case finding. *T. E. Osmond*

WONG, T. H. & WANG, P. N. **Venereal Disease among Prostitutes and Promiscuous Women in Taiwan.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 580–87.

In Taiwan there are licensed prostitutes and a number of others who practise unlicensed prostitution including entertainers, bar girls, tea-room girls and hotel maids; the licensed prostitutes are compulsorily examined monthly for syphilis and weekly for gonorrhoea and other venereal diseases. Treatment is compulsory for those found infected.

In a survey the following numbers were examined: Tainan 277, Keelung 200, Kaohsiung 437 and Taipei 100; the large majority fell in the age-groups 16–20 and 20–30.

The reactivity with the VDRL test was 10·6% in licensed prostitutes, 17·6% in entertainers, 14·7% in bar girls, 7·9% in tea-room girls and 21·6% in hotel maids; 8 licensed prostitutes had dark-ground positive sores. The prevalence of gonorrhoea ranged from 17·1% in bar girls to 41·2% in tea-room girls [why the difference should be so great is not clear] and most of those infected were aged 16–20 years. Genital ulcer was found in 2·1% of all cases and 40% of these were dark-ground positive. Condylomata acuminata were found in 8·8% and *Trichomonas vaginalis* in 1·7% of licensed prostitutes and in 27·8% of the other types [presumably prostitutes take more care of themselves].

A previous survey of unlicensed prostitutes showed a much higher incidence of venereal disease than that given in this paper. *T. E. Osmond*

OHNO, T., KATO, K., NAGATA, M., HATTORI, N. & KANEKAWA, H. **Prophylactic Control of the spread of Venereal Disease through Prostitutes in Japan.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 575–79.

It is calculated that there are 150,000 prostitutes in Japan and in 1956, 144,273 cases of venereal disease were traced to 14,294 contacts, 72% of whom were prostitutes or their male partners. Moreover, since brothels have been done away with the dispersal of prostitutes makes the tracing of infected women much more difficult.

As a result the prophylactic use of antibiotics appears to be the most effective way of controlling venereal disease. For this purpose vaginal foaming tablets were employed; these contained sodium bicarbonate, tartaric acid, boric acid, glucose, talc and starch, to which were added 50,000 units of penicillin or 100 mgm. of other antibiotics such as chlortetracycline, chloramphenicol or oxytetracycline.

For prophylaxis 1 tablet was inserted deep in the vagina after vaginal irrigation following the last sexual intercourse each night.

Various tests were carried out to calculate the concentration of the antibiotic in the vagina next morning and also the blood concentration. Details are set out in 2 tables.

Clinical tests were carried out on prostitutes after 1 penicillin tablet daily for a month and also after 1 tablet of 1 of 3 antibiotics daily for 3 months, with untreated controls. Results in the first test showed 1 case of gonorrhoea in 10 persons in the test group compared with 9 out of 20 in a control group; results of the second experiment were similar although oxytetracycline seemed less effective than penicillin or chloramphenicol.

Similar tests were carried out *vis-à-vis* syphilis; after penicillin 20 persons out of 20, after chloramphenicol 8 out of 9 and after oxytetracycline 5 out of 5 escaped infection as evidenced by negative serological examinations for 4 months; 6 out of 106 persons in a control group became seropositive within 4 months.

[This form of prophylaxis seems to have been fairly successful, but its efficacy depends first on finding the prostitute and secondly on ensuring that she inserts the tablet, neither of which is easy.] *T. E. Osmond*

Guthe, T. **Prevention of Venereal Infections.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 405–26, 2 figs. [33 refs.]

This long article sets out the views and suggestions of one of the world's greatest experts on venereal disease prevention. Under "A wider outlook" he deals in turn with levels of prevention, case finding, maternal and child health, armed forces, occupational health and prostitutes. Under "Prophylaxis and preventive treatment" he considers prevention, local and systemic prophylaxis of syphilis and the problem of gonorrhoea. 2 figures and 4 tables amplify the written word.

Epidemiological knowledge is a most important factor in the prevention of venereal disease; there are 5 levels of prevention: (1) health promotion, (2) specific protection, (3) early recognition and prompt treatment, (4) disability limitation, and (5) rehabilitation. Of particular importance are the advisability of obligatory blood testing of pregnant women, cooperation between the armed forces and civil medical authorities and implementation of the Brussels Agreement (because ports always harbour foci of infection). Prostitution varies in different areas; where it is rife regular inspection is helpful, but smears for the detection of gonorrhoea in females are often of little value and the subject needs more research.

Under prophylaxis and preventive treatment the prevention of congenital syphilis by treatment of the syphilitic pregnant woman is almost 100% effective; local prophylaxis is successful in proportion to the time and efficiency of application; systemic prophylaxis of syphilis can be carried out with bismuth, or better with penicillin, and this applies to yaws; whether the world decline in early syphilis is a "natural cycle" phenomenon is doubtful, but it is an attractive theory.

The reason why syphilis has declined much more than gonorrhoea since the introduction of penicillin is discussed at some length and this is worthy of careful study. Should the use of long-acting varieties of penicillin replace those which act quickly but only for a short time? One type seems desirable for syphilis and the other for gonorrhoea; there is no doubt that while the spirochaete remains very sensitive, the gonococcus is becoming more and more resistant, as was the case with sulphonamides. *T. E. Osmond*

Allen, R. H. & Tonks, D. B., with the technical assistance of Evelyn Fowler. **Pure Phosphatides and the Serodiagnosis of Syphilis. Relation of Chemical Structure to Reactivity.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 547–61. [33 refs.]

Much research has been carried out in order to find a suitable substitute for natural lecithin, and to a lesser extent for cardiolipin, in the preparation of antigens for the serodiagnosis of syphilis.

The work described in this article is so complicated and technical that only a few of the results can be given in a summary.

Of the substitutes for Pangborn lecithin lysolecithins, glycerylphosphorylcholine, glycollecithins, glycerophosphoric acid and cephalins were employed; substitutes for cardiolipin included glyceryl-glycerophosphoric acid, pentaoleoyl-bis-(L-α-glyceryl)-phosphoric acid, dipalmitoyl-bis-(glycol)-phosphoric acid, L-α-glycerophosphoric acid (substituted) and β-(dioleoyl-glycerophosphoric acid (monosodium salt).

The following combinations of synthetic compounds in place of cardiolipin and Pangborn lecithin were studied; (1) L-α-(dimyristoyl) glycerophosphoric acid and L-α-(dioleoyl)-lecithin, (2) monosodium salt of β-(dioleoyl)-glycerophosphoric acid and L-α-(dioleoyl)-lecithin and (3) tetramyristoyl-bis-(L-α-glyceryl)-phosphoric acid and L-α-(dioleoyl)-lecithin.

Results are set out in 4 tables.

In summary, dimyristoyl lecithin proved a suitable substitute for Pangborn lecithin, but none of the compounds lacking the complete lecithin structure was satisfactory; a satisfactory Kolmer antigen was prepared from stearoyl glycollecithin. When the choline group was absent reactivity was reduced with Kolmer antigen and absent with VDRL antigen; thus 2 fatty-acid groups and the choline group are necessary. It is possible that the action of lecithin is only physical, *i.e.* it acts as an emulsifying agent. No really satisfactory substitute for cardiolipin has been found, but the sodium salt of β-(dioleoyl)-glycerophosphoric acid shows promise and is worthy of further study.

T. E. Osmond

Schmidt, H. & Bentzon, M. W. **Investigations on the Rapid Plasma Reagin Test.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 563–8, 1 fig.

The use of plasma in place of serum for diagnostic tests for syphilis has already been reported [this *Bulletin*, 1958, v. 33, 226]. These authors used potassium sequestrene (obtained by the action of potassium hydroxide on ethylene diamine tetra-acetic acid) as an anticoagulant and used plasma so obtained for slide

tests for syphilis, comparing results with the VDRL test. Antigen for the plasma test was prepared as follows: 5 ml. of freshly prepared antigen suspension (cardiolipin 1, lecithin 9, cholesterol 30) were centrifuged for 15 minutes at 3,000 r.p.m.; the supernatant was removed and the sediment was resuspended in 5 ml. of 10% choline chloride solution; when used at once this was called "fresh" RPR antigen and after storage for 4–5 days at 4°C. "old" RPR antigen.

Specimens of serum and plasma from 51 patients with syphilis and 86 patients who were healthy or suffering from diseases other than syphilis were tested in parallel with the 2 RPR antigens and ordinary VDRL antigen. Plasma samples were obtained by adding about 8·5 ml. of patient's blood to a tube containing 0·17 ml. of a 5% solution of sequestrene and inverting the tube 10 times. Samples were centrifuged for 5 minutes at 3,000 r.p.m. [one of the advantages that have been claimed for plasma tests is that centrifuging is not necessary].

In 45 syphilitic sera both types of RPR antigen gave higher titres with plasma than ordinary VDRL antigen with serum; "fresh" RPR antigen was more active than "old" antigen; of 90 samples from presumably seronegative persons 4 turned out to be syphilitic and were positive with all tests, 1 was negative with fresh RPR antigen and doubtfully positive in VDRL test and the remainder were negative in both plasma and serum tests.

Thus RPR antigen tests with plasma appeared to be more sensitive and no less specific than ordinary VDRL tests. *T. E. Osmond*

PAVLATOU, M., MARCELOU, U. & TRIANTAPHYLLI, I. [L'antigéne tréponémique—souche Reiter dans la sérologie de la syphilis] **[Treponemal Antigen prepared from the Reiter Strain in the Serology of Syphilis]** *Acta Microbiologica Hellenica.* Athens. 1958, Mar.–June, v. 3, Nos. 2–3, 79–88. [31 refs.] [In Greek.] French summary.

The authors, in Greece, carried out complement-fixation tests with a Reiter strain antigen in parallel with the classical serological tests (cardiolipin complement-fixation and Kahn standard tests) and with the TPI test. 443 sera from patients with syphilis, pregnant women and patients with diseases other than syphilis were examined.

The Reiter antigen was more specific in complement fixation than the lipid antigens. For example, it was positive in only 10 cases of 147 which were positive with one or other of the lipid antigens and negative to the TPI. In the whole 443 sera it gave only 2·25% false positive results, while the lipid antigens gave 33·18%.

The Reiter antigen was less sensitive than the TPI and sometimes than the lipid antigens in old fully treated cases of syphilis. In 73 cases where the TPI was positive, the Reiter antigen showed only 54 positives. It was less sensitive than the TPI in 4·28% as were the lipid antigens in 3·16%, in the whole 443 sera.

The authors recommend that the complement-fixation test with Reiter antigen should be used in parallel with the lipid antigen tests as a routine, especially when the TPI test is not done. In most cases this combination will probably elucidate false positive results. *H. J. O'D. Burke-Gaffney*

DAGUET, G. L., PILLOT, J. & FAURE, M. Étude d'antigènes tréponémiques (souche Reiter) employés dans la réaction de fixation du complément pour le sérodiagnostic de la syphilis. **[Study of *Treponema* Antigens (Reiter's Strain) used for the Sero-Diagnostic of Syphilis by means of the Complement-Fixation Reaction]** *Ann. Inst. Pasteur.* 1958, Oct., v. 95, No. 4, 463–73. [10 refs.]

Reiter antigens, consisting of whole treponemes, protein extracts free from lipoids and purified protein extracts, were tested in parallel with cardiolipin antigens in complement-fixation reactions (Kolmer) and with the Kline flocculation and TPI tests. 293 sera, including 94 from normal persons, 184 from syphilitic persons and 25 from persons giving biologically false positive reactions [these appear to add up to 303] were tested.

In the first series of 116 sera Reiter antigen IP [Institut Pasteur] 10 appeared more specific than cardiolipin but less sensitive in early syphilis and more sensitive in late and latent syphilis and nearer to TPI than cardiolipin.

In a second series of 70 sera antigen IP 17 gave results similar to those with IP 10.

In a third series of 107 sera antigens IP 21, 22, 24, 25 and 26 all gave similar results.

In a fourth series of 10 sera from patients with secondary syphilis Reiter antigens proved inferior to cardiolipin.

In a fifth series a mixture of syphilitic sera was titrated with cardiolipin and 5 Reiter antigens in parallel; the latter showed no significant differences between themselves but all were inferior to cardiolipin.

It is concluded that the various Reiter antigens tend to give similar results, keep well at ice-chest temperature, are more specific than cardiolipin but less so than TPI, are less sensitive than cardiolipin but often more sensitive than Kline antigens and are reproducible. They should be employed particularly in the case of "problem" sera.

(Whole treponeme antigens include IP 22 and 25. Lipoid-free protein extracts include IP 10, 17 and 21. Purified protein extracts include IP 24 and 26.)

T. E. Osmond

RANQUE, J. & DEPIEDS, R. Influence du CO_2 sur le phénomène d'immobilisation spécifique des Tréponèmes. **[The Influence of CO_2 on the Phenomenon of Specific Immobilization of Spirochaetes]** *C.R. Soc. Biol.* 1957, v. 151, No. 7, 1404–6.

In order to account for certain discordances in the results of TPI tests when repeated, these authors tested the effect of pressure of nitrogen and CO_2.

8 of 11 sera showed a very marked fall in the level of immobilization when the pressure was changed from just above atmospheric to 0·500 kgm. per sq. cm. When the pressure was reduced to 0·250 kgm. per

sq. cm. similar, but less marked, suppression of immobilization occurred in all of 8 sera tested; when the pressure was 0·100 kgm. per sq. cm. results were very variable in 8 sera, all showing some, but only 2 marked, suppression.

Possible explanations are (1) action on antibody, (2) action on complement; the latter seems the more probable since, when a haemolytic system was added at the end of the operation under a pressure of 0·500 kgm. per sq. cm., little if any haemolysis occurred; at a pressure of 0·250 kgm. per sq. cm. a good deal of haemolysis occurred and at 0·100 kgm. per sq. cm. it was complete.

Thus it seems that under pressure of CO_2 complement cannot act and immobilization does not take place even though the complement has only been suppressed but not destroyed. The moral seems to be to avoid a high pressure of nitrogen and CO_2.

T. E. Osmond

HACKETT, C. J. & GÖCKEL, C. W. **Equipment and Technique of Intramuscular Injection in Mass Treatment Campaigns against the Treponematoses.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 531–45, 8 figs.

It seems that the technique of intramuscular injections (usually of penicillin), although well known, varies a good deal in different field campaigns and with different teams. This article explains very clearly the equipment needed and its maintenance with special reference to syringes and needles, sites of injection, preparation of the patient and any necessary after-treatment.

Strict attention to technique is necessary if accidents are to be avoided; abscesses at the site of injection, intravenous injection, injury to nerves and causing unnecessary pain can all be avoided by careful attention to detail.

The sections on the sharpening of needles and sterilization of syringes are particularly good but stress might have been laid on the avoidance of virus hepatitis resulting from infected syringes; incidentally an intramuscular needle rather than a "hypodermic" needle should be employed (*vide* Fig. 4).

The information in this article should be of great value to all who are not already expert in the matter.

There are 8 excellent illustrations. *T. E. Osmond*

ŻÓŁKIEWICZ-RODZIEWICZ, Helena & RODZIEWICZ, J. Leczenie kiły układu nerwowego na podstawie materiału Kliniki Dermatologicznej Akademii Medycznej w Lublinie w latach 1949–1954. [**The Treatment of Neuro-Syphilis, on the Basis of the Material of the Dermatological Clinic of the Medical Academy in Lublin, in the Years 1949–1954**] *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1957, v. 12, 277–80.

The English summary appended to the paper is as follows:—

"Using the analysis of the cerebrospinal fluid as criterion, the authors present the results of penicillin, bismuth and salvarsan treatment of lues nervosa. The clinical material comprised 208 cases with various forms of syphilis of the nervous system: Lues nervosa asymptomatica 43, Lues meningo-vascularis 67, Tabes dorsalis 87, Paralysis progressiva 8, Taboparalysis 3. The evaluation of the results of treatment concerns only 146 patients with changes in the cerebrospinal fluid, in whom a check-up examination of the fluid was carried out after the treatment. During treatment the patients were given from 4 to 36 millions of penicillin units and an average of 2 to 5 salvarsan-bismuth or bismuth cures.

"In 34 cases the treatment proved ineffective: in 9 patients an almost complete improvement was obtained, in 22 no improvement was noted, in 3 an aggravation followed. Best results were obtained in lues nervosa asymptomatica—normalization of the cerebrospinal fluid in 89.18 per cent: not so good were the results in lues meningo-vascularis—78.04 per cent; in tabes dorsalis the percentage was only 68.7."

GUTHE, T., IDSÖE, O. & WILLCOX, R. R. **Untoward Penicillin Reactions.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 427–501. [Numerous refs.]

This is a very long communication and is well documented, as evidenced by more than 500 references.

The most serious problems as regards penicillin reactions are anaphylaxis, superinfection with a penicillin-resistant organism and cross infection with the same organisms (which might cause great harm to the community). In the early days toxicity was largely due to impurities but these have largely been eliminated; however, reactions do occur and may be the result of various interacting causes, most of which lie within the patient himself; reactions may be local or systemic, the latter being the more serious. Overgrowth of non-susceptible organisms (*e.g.* staphylococcus), including superinfection and cross infection, and overgrowth of monilia must be kept in mind.

Allergic skin reactions are the most common and include contact dermatitis, urticaria, angio-oedema and serum-sickness-like reactions. Anaphylaxis is the reaction most to be feared and is said to be responsible for 0·1–0·3 deaths per million injections. Such reactions can be largely avoided by enquiry as to previous sensitivity to penicillin or an allergic diathesis and the use of single injections or short courses; treatment is that of shock and adrenaline may be life saving; desensitization and the use of penicillinase have their uses; skin tests seem to be of doubtful value, and a positive test is more valuable than a negative one.

In general, certain precautions should be taken when using penicillin: (1) do not use it unless there are clear indications; (2) always enquire as to previous sensitivity before giving an injection; (3) see that the injection is deep and intramuscular; (4) be ready to deal with anaphylactic shock (have adrenaline available); (5) in mass campaigns rely as far as possible on single injections.

There is no doubt that penicillin is the most abused drug of modern times; the public should be told that it is not a "cure-all"; it should not be used indiscriminately. *T. E. Osmond*

WILLCOX, R. R. **Clinical Problems in the Antibiotic Treatment of Gonorrhoea.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 503–17. [51 refs.]

Evidence is accumulating that the gonococcus is becoming, at least partially, resistant to penicillin. In the early days of penicillin the cure rate was 90–100% yet although early syphilis has fallen to 5% of the wartime peak, the corresponding figure for gonorrhoea is only 50% and during the last few years its incidence has increased in many countries. It does seem that the repository penicillins are less successful than the quickly acting ones. The criteria of failure of cure or reinfection are somewhat hazy, but generally speaking rather more than half the patients seen after treatment are relapses and rather less than half reinfections. Much depends on the period and efficiency of observation; theoretically the observation period should be 3 months (to exclude concomitant syphilis) but few patients will attend for so long and 3 weeks appears to be a more suitable period. Oral penicillin gives good results but is expensive; much the same applies to several other antibiotics, especially streptomycin, but some of them too are expensive and the routine use of streptomycin on a large scale might lead to drug resistance.

It is concluded that, although there is evidence of some resistance to penicillin, it is not likely to be anything like as great as it is to sulphonamides, that penicillin preparations which give a rapid high serum level should be employed in adequate doses in preference to repository preparations and that in any case other antibiotics are available in cases of penicillin failure. The outlook therefore is not so black as it is sometimes painted.

Incidentally, although penicillin should not be used routinely for prophylaxis, a case can be made out for its use in prostitutes where they are known to be the chief sources of infection. *T. E. Osmond*

WILLCOX, R. R. **Failures in the Treatment of Gonorrhoea in Ethnic Minorities.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 3, 569–74. [Refs. in footnotes].

This article deals mainly with the results of the treatment of gonorrhoea in whites and non-whites (mainly West Indians and West Africans) in England and Wales in recent years. It is stated that there are now 100,000 West Indians in Great Britain. In 1956 Negroes represented 0·2% of the total population yet they accounted for 14·6% of the gonorrhoea cases studied by the British Co-operative Clinical Group [this *Bulletin*, 1956, v. 31, 1006] [this gives a false impression since the Negroes in this group were mostly adult males whereas the indigenous population included men, women and children]; however, in London the proportion of Negroes among patients suffering from gonorrhoea has risen from 8·5% in 1952 to 56% in 1957. Failure rates were twice as high in Negroes as in whites during 1956–57 irrespective of the type of treatment; there are 3 possible explanations: (1) the gonococcus is becoming more resistant in Negroes, (2) penicillin is absorbed more slowly or excreted more rapidly in these persons, (3) many so-called failures are in fact reinfections.

It does seem clear that the gonococcus (or at least some strains) is becoming less sensitive to penicillin as shown by the fact that slowly absorbed repository preparations with relatively low serum levels are less effective than non-repository preparations which give a high initial level.

Relapses and reinfections are greater in non-whites than in whites; in non-whites 125 out of 218 relapses (57·3%) occurred within a week compared with 98 out of 114 (85·9%) in whites; thus relapses are commoner in non-whites than in whites and tend to occur later.

It is evident that gonorrhoea in the ethnic minorities (West Indians and West Africans) in Britain presents an ever increasing problem. *T. E. Osmond*

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows:— Tetanus; other diseases.

DA MOTTA, L. C. Tétano. Estudo da evolução da sua mortalidade em Portugal e (Continente e Ilhas Adjacentes) durante os anos de 1955 e de 1956. Importância da sua profilaxia pela vacinação. [**Tetanus; Incidence and Mortality in Portugal and the Adjacent Islands in 1955–56; Importance of Immunization**] *Bol. Serviços de Saúde Pública.* Lisbon. 1957, Oct.–Dec., v. 4, No. 4, 477–506, 1 coloured folding map. English summary.

The author remarks that a previous paper by him on tetanus in Portugal [this *Bulletin*, 1957, v. 32, 571] contained many errors, and in the present paper he enlarges his data. The death rates from tetanus per 100,000 in 1955 were for the mainland 3·69 and for the islands (Azores and Madeira) 5·45; the only real change for 1956 was a reduction to 3·6 in the islands.

Nearly 70% of the deaths were in persons under 20 years old, and about 50% were in infants under 1. Rural workers, housewives and servants had high rates, representing almost 30% of all the deaths.

The author advocates immunization with triple vaccine (whooping cough, diphtheria and tetanus) at the age of 3–6 months, with 3 doses at intervals of 1 month, and a booster dose a year later and again at school age, and on entering military service—in other words at intervals of 5 years. He also advocates it particularly for pregnant women and people in certain occupations in which the risk is greatest.

Charles Wilcocks

TAKOS, M. J. **Tetanus as a Concomitant of Work Accidents in Tropical Countries.** *Indust. Med. & Surgery.* Miami. 1958, Oct., v. 27, No. 10, 518–19.

This is a study of 170 cases of tetanus occurring in Dade County, Florida, from 1943 to 1957; 93 patients died. The length of incubation was closely related to mortality in 76 patients where the incubation period

could be established. Puncture wounds and minor lacerations accounted for nearly 90% of the traumatic cases. No special industrial factor was involved nor were outdoor work and contact with the soil always factors. It is impossible to decide which wounds are infected and which are not, and the usual dose of 1,500 units prophylactic antitoxin does not always protect. Active immunization with a booster dose every 3 years is the only way to protect workers.

A. B. Christie

WILKENS, G. L. Behandeling van zeer ernstige vormen van tetanus met spierrelaxantia en kunstmatige ademhaling [**Treatment of Tetanus with Muscle Relaxants and Artificial Respiration**] *Nederl. Tijdschr. v. Geneesk.* 1958, Feb. 22, v. 102, No. 8, 375–9. [28 refs.] English summary (3 lines).

A description is given of the treatment of 3 patients suffering from tetanus. (1) A man aged 21, who developed tetanus 6 days after a wound from a saw in spite of treatment with antiserum. It was not possible to suppress the convulsions with succinylcholine, and an infusion of *d*-tubocurarine was given in a dose of 12 mgm. per hour. High tracheotomy was carried out, and respiration was given through the cannula by a constant pressure apparatus (Poliomat). The alveolar carbon dioxide content was regulated to 5·6% with the aid of an infra-red meter and the arterial oxygen saturation was controlled with an oximeter. By the 21st day of illness treatment with *d*-tubocurarine could be discontinued, by which time the patient had received 6·32 gm. (2) A man aged 50, who developed tetanus 7 days after an axe wound on the hand; 30,000 units of antiserum had been given. *D*-tubocurarine was given at the rate of 15 mgm. per hour in a total dose of 5·14 gm. over 13 days, with artificial ventilation as in case 1. (3) A boy aged 7, who developed tetanus 9 days after wounding a finger between the cogs of a domestic wringer. An intravenous infusion of *d*-tubocurarine was given at the rate of 10 mgm. per hour, in a total dose of 1·8 gm. over a period of 12 days. Artificial respiration was also carried out. After recovery the patients were questioned about their experiences during treatment, and it was found that they had not experienced any mental trauma in spite of the lack of narcotic treatment. The success of the treatment is ascribed to the use of continuous artificial respiration as carried out in a specialized centre.

D. J. Bauer

KRANENDONK, O. Listeriosis bij moeder en kind. [**Listeriosis in Mother and Child**] *Nederl. Tijdschr. v. Geneesk.* 1958, June 21, v. 102, No. 25, 1202–6, 2 figs. [27 refs.] English summary (8 lines).

A case of *Listeria monocytogenes* infection of a parturient woman and her infant is described. The course of the pregnancy was normal and delivery occurred at term. On the 4th day of life the infant ceased feeding and developed a generalized punctate exanthem; death occurred shortly afterwards. *L. monocytogenes* of type IVb was isolated from the cerebrospinal fluid. The course of the puerperium was normal, but organisms resembling *L. monocytogenes* were seen in vaginal smears and could be isolated in culture up to the 3rd week after delivery. The isolation was facilitated by making subinoculations at intervals from a glucose-broth culture of the test material kept at 4°C.

D. J. Bauer

VAN DRIEST, G. W. & KAMPELMACHER, E. H. Een zuigeling met meningitis veroorzaakt door *Listeria monocytogenes* type-II. [**Meningitis due to *Listeria monocytogenes* Type II in a Baby**] *Nederl. Tijdschr. v. Geneesk.* 1958, June 21, v. 102, No. 25, 1206–7. English summary (6 lines).

An infant aged 3 months developed an acute illness with vomiting, opisthotonus and a suppurative discharge from the umbilicus. Examination of the cerebrospinal fluid showed pleocytosis and the Nonne and Pandy reactions were strongly positive; the white cell count was 13,000 with 3% monocytes. From the umbilicus and cerebrospinal fluid *Listeria monocytogenes* type II was isolated. The strains were sensitive to the usual antibiotics, but in spite of treatment with streptomycin, penicillin and oxytetracycline the condition deteriorated, convulsions developed and death occurred on the 8th day of illness. The case of listeriosis described is the 4th known instance of human type II infection.

D. J. Bauer

MEYER, P. & MOESCHLIN, S. Das Lymphdrüsenpunktat der Katzenkratzkrankheit. [**Lymph Gland Puncture in Cat Scratch Disease**] *Schweiz. med. Woch.* 1958, Oct. 18, v. 88, No. 42, 1070–71, 3 figs. on pl. p. 1058.

Gland punctures were taken and a gland removed for biopsy in a case of cat scratch disease confirmed by the intradermal test.

Histological examination of sections from the lymph node showed that it was surrounded by a firm capsule and the architecture destroyed. There were nodules of epithelioid cells, the centre of which were necrotic and infiltrated by polymorphonuclear cells. These abscesses were separated from the epithelioid cell layer by firm connective tissue. Giant cells were not seen in the preparations, although in other cases when they are present they are of the foreign body type. These areas of necrosis may coalesce, forming peculiar characteristic band-like structures. In early cases granulomatous changes are more prominent but in later cases abscess formation is more marked.

Smears from gland puncture showed a variegated picture. There was an increase of reticular elements —large reticulum cells with scanty bluish staining protoplasm and large nuclei often eccentric with bluish nucleoli. Various transition forms were seen between these young large reticulum cells and the older epithelioid cells. These latter were reminiscent of the epithelioid cells of tuberculosis or of Boeck's disease. Occasionally the young large reticulum cells were undergoing necrosis and then they resembled Hodgkin's cells. Sinus endothelial cells, multinuclear reticulum cells frequently in mitosis and numerous macrophages completed the picture.

Such a picture is difficult to differentiate from early Hodgkin's disease or tuberculosis particularly in the

early stages. In Hodgkin's disease the nucleoli are larger and not so sharply defined as in cat scratch disease and there are some slight differences in the chromosomes of cells in mitosis.

Owing to the possibility of misinterpretation of the picture given by lymph node puncture in cat scratch disease, histological examination of an excised lymph node should always be carried out.

P. A. Clearkin

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order:—General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

LAMB, R. **Occupational Hazards in the Bone-Meal Industry.** *Lancet.* 1958, July 19, 151–53.

The hazard is anthrax. In one factory in Greenock bones are imported from India, Pakistan and Argentina, and are crushed to provide material for animal charcoal. Throughout the factory there is a very fine bone dust, and anthrax spores have been found in this and in the crushed bones. The author reports 4 cases of cutaneous anthrax in factory workers in the period 1955–8 (1 patient was a woman employed in repairing sacks); all were treated with penicillin and cured. He also describes 2 cases of empyema in exposed persons; clostridia were isolated from the pus, but not anthrax bacilli.

Charles Wilcocks

GREEN, D. M. & JAMIESON, W. M. **Anthrax and Bone-Meal Fertiliser.** *Lancet.* 1958, July 19, 153–54.

The authors [this *Bulletin*, 1955, v. 30, 507] have already reported 6 cases of anthrax in persons handling bone meal; they now report 4 other cases of cutaneous anthrax in Dundee, 3 in persons handling bone meal and 1 in a veterinary surgeon. Anthrax bacilli were isolated from bone fibre used by one of the patients; the technique is described. All isolated strains were sensitive to several antibiotics, and the 3 patients described recovered after treatment with penicillin or penicillin and streptomycin. No details are given of the disease in the veterinary surgeon, who was infected by an animal.

Charles Wilcocks

ÖZLÜARDA, D. Memleketimizin bazi bölgelerinde Brucellergen ve aglütinasyon testleri ile Brucellos arastirmasi ve bu testlerin epidemiyolojik degeri hakkinda bir çalisma. [**An Investigation on Brucellosis in some Area of Turkey with Brucellergin and Agglutination Tests; Epidemiological Value of these Tests**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1957, v. 17, No. 3, 196–207. [10 refs.] English summary.

The brucellergin skin test was applied to 1,560 persons in various areas (Konya and Zonguldak; Ankara and Bursa) and 22% were found positive, the rates in Ankara and Bursa where there is much animal husbandry being twice as high as in the other places. Women are commonly positive, and they have as much contact as men with cattle and sheep. The highest rates were in persons aged 20–40.

The brucellergin test is claimed to be specific, but it was found that only 9·7% of subjects positive to this test showed agglutinins at titres of 1 in 60 or more. If the agglutinin test only had been used, therefore, 90·3% of the infected persons would have been missed. There was no relation between the size of the local skin reaction and the agglutinin titre. 50% of patients suspected clinically of brucellosis gave positive skin tests.

Charles Wilcocks

AKYAY, N. & GÜRSEL, A. Bir Brüsella salgini ve Türkiye'de Brucellose. [**An Epidemic of Brucellosis in Turkey**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1957, v. 17, No. 3, 208–16. French summary.

In 1957 an outbreak was reported, in the personnel of a stock farm of the Ministry of Agriculture, of a disease which had been diagnosed as typhoid or paratyphoid fever but which serological investigation showed to be brucellosis; of 203 persons in the farm 47 were serologically positive and 25 sick persons were diagnosed clinically.

Serological examination of the sheep of the establishment revealed that 13·2% were positive for brucellosis, and it was established that the human outbreak was due to consumption of milk and milk products from the sheep. Official statistics hardly mention brucellosis in Turkey, but the present findings indicate that it is probably widespread.

Charles Wilcocks

AWAD, N. A. **Hepatic Function in Egyptians with Brucellosis.** *J. Trop. Med. & Hyg.* 1958, Nov., v. 61, No. 11, 274–9. [50 refs.]

The author reviews the reports of hepatic changes in human and experimental brucellosis. The production of characteristic brucellar granulomata appears to have been clearly established [BARRETT and RICKARDS, this *Bulletin*, 1954, v. 29, 362] and cirrhosis of the liver after brucellosis or in conjunction with it has been reported on a number of occasions.

The author reports the results of an investigation into the liver functions, as revealed by a series of tests, of 21 adult male Egyptians, in whom the diagnosis of brucellosis had been confirmed by the recovery of *Br. melitensis* from the blood or urine as well as by the demonstration of a high serum agglutination titre.

The liver function tests employed on the sera were: zinc, thymol and phenol turbidity, bromsulphthalein retention, serum bilirubin, cephalin flocculation, cholinesterase and estimations of proteins and their electrophoretic fractionation.

Values for these tests were first determined on a group of apparently normal Egyptians and a comparable group of Europeans resident in Egypt. These tests showed the mean levels for the zinc turbidity and bromsulphthalein retention tests were significantly higher in the Egyptians but those of the cephalin flocculation test and total plasma proteins were lower. In as far as these tests may indicate liver disease in Egyptians this may be attributable to schistosomiasis. In the patients with brucellosis it was found that the zinc and thymol turbidity tests were raised considerably above normal levels whereas the phenol turbidity and cephalin flocculation levels either remained unchanged or were slightly less than normal. These results indicate increased gamma globulin formation. The zinc and thymol turbidity levels were not materially lowered during antibiotic therapy. The total serum protein level remained unchanged. Bromsulphthalein excretion and serum cholinesterase levels were lowered during the acute phase but returned to normal with the cure of the disease. It is suggested that some persistent or residual liver affection may occur resulting in increased formation of gamma globulin.

[A well-controlled series of observations.]

Frederick J. Wright

IPP, H. **Brucellar Spondylitis and Hepatitis. A Report on Two Cases with a Review of the Literature.** *South African Med. J.* 1958, Nov. 8, v. 32, No. 45, 1077–8, 1 fig. [12 refs.]

The author draws attention to the occurrence of brucellosis in South Africa. He records the case of a female aged 65 years suffering from pain in the lower limbs for 3 months and who was diagnosed as suffering from a degenerative disc lesion but 47 days treatment was of no avail and she was found to be febrile. An X-ray showed a destructive lesion of the disc and adjacent end-plates at the second lumbar interspace. Modified Coombs tests for brucellosis were positive and the patient responded well to antibiotic therapy. The second case recorded is that of a female aged 49 years, from a farm, suffering from fever, upper abdominal pain and presenting spider naevi on the chest and tenderness of a liver enlarged 3 fingersbreadth. Liver function tests showed considerably impaired function. A modified Coombs test was positive. It appears that the patient before brucellosis was diagnosed did not respond to broad-spectrum antibiotics but subsequently did so.

[This is further evidence of the interest being taken in South Africa in brucellosis, see ZOUTENDYK (this *Bulletin*, 1958, v. 33, 1131)].

The first case illustrates one manifestation of brucellosis but the author is not correct in implying that cultures are usually negative when brucellosis affects the spine. With regard to the second case, although hepatic changes in brucellosis have been studied, the impaired liver function recorded can only doubtfully be attributed to brucellosis. See WRIGHT *et al.* (*ibid.*, 1954, v. 29, 812) and AWAD (see above).]

Frederick J. Wright

BROOM, J. C. **Leptospiral Infection Rates of Wild Rats in Britain.** *J. Hygiene.* 1958, Sept., v. 56, No. 3, 371–6, 1 map.

In 1953, the author, with GIBSON, made a survey of *Rattus norvegicus* from a rural area in Wales, to determine their rate of infection with *Leptospira icterohaemorrhagiae* [this *Bulletin*, 1954, v. 29, 46]. He has now extended the study to widespread areas of Britain and the material included *R. norvegicus* and *R. rattus*, some alive and some dead, and a separate study of *R. rattus* from fumigated ships. The areas covered are shown in a map.

Kidneys from dead rats were received in formol saline and half of each kidney was stained by silver impregnation and examined for leptospires. Specific identity was not of course possible in microscopic preparation, but it was assumed that the leptospires found in *R. norvegicus* were *L. icterohaemorrhagiae* as all strains from living rats in Britain so far have been found to belong to that type.

850 dead *R. norvegicus* were examined (403 from rural and 447 from urban areas) including sewer rats. 370 (43%) were positive for leptospires, irrespective of habitat. There were some local variations, which are shown in a table: these fluctuated between 30% for London, the Home Counties and East Anglia on the one hand and 75% in South Wales on the other. In individual towns, which are listed, the percentages varied between 10 and 75. There was little sex difference in the infection rate, but an unexpectedly high rate was found in young rats—35% of 222, compared with 46% of 628 adult rats. This is discussed with reference to the literature and it is concluded that there was no evidence that a low rate of infection was associated with sexual immaturity.

219 *R. norvegicus* were caught alive, 97 from refuse destructors in a Midland town and 122 from 3 London domiciliary boroughs. Agglutination tests and culture of kidneys for leptospires were performed. 93 (43%) were positive, 45 by both methods, 28 by agglutination only and 20 by culture only. The kidneys of 69 Midland rats were also examined microscopically. The overall result of all 3 methods of examination in this case was that 39 (55%) were positive. Of the 65 strains of leptospires isolated, all were *L. icterohaemorrhagiae*. The subtype was determined in 50 and this was (AB) in 30 and (A) in 20.

R. rattus is now believed to be found only in or near ports or large towns. Kidneys were examined from 123 rats of this species (88 from London, of which 75 were alive). The results of the microscopic examinations were: London 0/88, Cardiff 16/19, Liverpool 13/14, Wolverhampton 2/2 positive. 1 strain was isolated from kidney culture: serum from this rat and 1 other had antibodies for *L. icterohaemorrhagiae*, so that the positives from London were 2/88. *R. rattus* is not usually regarded as the host of election for *L. icterohaemorrhagiae* and the London rates conform to this, but the proportion of leptospire infections in the other towns is quite abnormal.

There were 69 positive results in the examination of kidneys from 98 rats taken from fumigated ocean-going steamers. It was ascertained that the ships had

called at ports in North, West and South Africa, India, North and South America and Australia. It was not therefore possible to determine the exact origin of these infections. *H. J. O'D. Burke-Gaffney*

Broom, J. C. & Coghlan, Joyce D. *Leptospira ballum* **in Small Rodents in Scotland.** *Lancet.* 1958, Nov. 15, 1041–2.

The authors report the first isolation of *Leptospira ballum* in Britain. Serological and cultural examinations were made of 162 rodents trapped near Edinburgh. Some strains of leptospires from mice were extremely slow to develop and kidney cultures in Korthof's medium were kept for 3 months before being discarded. 4 strains of *L. ballum* were isolated from 2 wood-mice (*Apodemus sylvaticus*), 1 field vole (*Microtus hirtus*) and 1 bank vole (*Clethrionomys glareolus*). In addition 6 strains of leptospires from the field vole and bank vole were related to *L. sejroe* and *L. saxkoebing* but were considered to be probably not identical with either; 2 of these rodents and 5 others (from which no leptospires were cultured) possessed agglutinins for *L. sejroe*; of the latter 5, 1 also had agglutinins for *L. bataviae* and one for *L. grippotyphosa.* Agglutinins were not detected in 12 of 15 murine renal carriers of leptospires and the authors concluded that serological surveys on small rodents may therefore be misleading.
J. G. P. Hutchison

Plesko, I., Kmety, E. & Bakoss, P. Výsledky prieskumu prírodného ohniska leptospiróz v oblasti Opavy. [**Results of Leptospirogical Investigations in the Region of Opava**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 6, 403–6.

The English summary appended to the paper is as follows:—

"By investigations of leptospira carriers in the region of Opava during the years 1956/57 11 strains of L. grippotyphosa, mainly from Micr. arvalis (6 strains), farther from Clethr. glareolus (3 strains), from Apod. flavicollis and Apod. agrarius one strain could be isolated. In serological and culture tests 2—8.1%, average 5.4% of the animals were positive during the two years. These findings show, that during an increasing epizootic an irradiation of the epizootic process from the main host to the other species living in the same biotope may be observed. The region of Opava is in the time being a monovalent focus of field fever."

Havlík, O. & Hübner, J. Isolace leptospiry *L. grippotyphosa* z lasičky, *Mustela nivalis.* [**Isolation of** *Leptospira grippotyphosa* **from** *Mustela nivalis*] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 6, 407.

The English summary appended to the paper is as follows:—

"Out of six weasels Mustela nivalis caught in the focus of L. grippotyphosa in North-West of Bohemia, in one case a positive cultivation of Leptospirae isolated from kidneys succeeded. The strain of Leptospirae was determined as L. grippotyphosa by agglutination—lysis with hyperimmune serums of rabbits. So the number of hitherto known reservoirs is enlarged by a new species."

Laurentz, F. K. **Public Health Significance of Psittacosis.** *Indust. Med. & Surgery.* Chicago. 1958, Apr., v. 27, No. 4, 175–6.

Turkeys have been implicated as sources of psittacosis since 1948, and several outbreaks of human disease originating from them have been recorded; the author reports 1 outbreak of 29 confirmed cases in Houston, Texas, in 1956. 2,000 turkeys were received for slaughter and within a few days the human disease began to appear in the employees in the slaughtering section. The slaughtered birds had been kept in cold storage and were then impounded; psittacosis virus was isolated from 4 of the birds in a random sample. The entire group of slaughtered birds was condemned and sent to a rendering plant.

There were still 4,000 live turkeys in the same flock; these were examined and evidence of psittacosis was found. The birds were then put on intensive treatment for a month [no details are given but one may presume that a wide-spectrum antibiotic was used] and 200 were examined with negative results. The flock was then regarded as free, and no other cases have been reported.

A table shows that in the United States 137 human cases reported in the first 38 weeks of 1958 could be attributed to poultry and 259 to psittacine birds. People employed on farms rendering or processing plants, or other marketing organizations, are particularly exposed. For protection of the public all birds for human consumption should be inspected.
Charles Wilcocks

Leachman, R. D. & Yow, E. M. **The Epidemiology of Psittacosis and Report of a Turkey-Borne Outbreak.** *Arch. Intern. Med.* 1958, Oct., v. 102, No. 4, 537–43, 1 fig. [46 refs.]

This paper describes yet another outbreak of psittacosis in man having its origin in turkeys. It occurred in the 41 employees of a poultry processing plant, 20 of whom had a clinical condition resembling psittacosis. The first cases occurred 1 week after the delivery of a certain batch of turkeys and complement-fixation tests showed a rising titre of psittacosis antibodies in 13 of the 20 affected members of the staff. The virus was isolated from frozen dressed turkeys and also from live birds on the farm from which the turkeys came. *S. P. Bedson*

Morimoto, T., Omori, T., Ishii, S. & Matumoto, M. **Miyagawanella: Psittacosis-Lymphogranuloma Group of Viruses. 6. Detection of Indirect Complement Fixing Antibodies against Psittacosis in Chicken Serum.** *Japanese J. Exper. Med.* 1958, June, v. 28, No. 3, 213–24. [30 refs.]

The allantoic fluid from hens' eggs infected on the 9th day of incubation and collected at death was used

as antigen after clarification by low-speed centrifugation. It was stored at −20°C. and used unheated. The inhibitory action of chicken antibody was examined at different temperatures—56°C. 1 hour; 37°C. 1 hour; 4°C. 5 hours; 4°C. 18 hours—and 1 hour at 37°C. was selected as the most suitable. Sera prepared against psittacosis virus in pigeon, guineapig, mouse, dog, cat, pig, goat and horse and naturally occurring antibody in man were examined as indicator sera. Those prepared in pigeon, dog and guineapig were the most satisfactory (they had the highest complement-fixation titres). Titration of the inhibitory action of chicken antibody was made both by dilution of complement and by dilution of the chicken serum, with very similar results. Sera from 103 fowls at the National Institute of Animal Health, Tokyo, were examined; 68 were negative and 33 had titres of 1 in 2 to 1 in 16; 2 were anticomplementary. *S. P. Bedson*

INABA, Y., OMORI, T., MORIMOTO, T., KUROGI, H., KONO, Y., ISHII, S. & MATUMOTO, M. **Miyagawanella: Psittacosis-Lymphogranuloma Group of Viruses. 7. Psittacosis Virus in Japanese Pigeons.** *Japanese J. Exper. Med.* 1958, June, v. 28, No. 3, 225–42, 2 figs. on pl. & 1 text fig. [28 refs.]

Psittacosis antibody has been demonstrated in Tokyo pigeons. Of 61 sera examined by the technique of haemagglutinin inhibition, 33, or 54·1%, had titres of 1 in 40 or over. 33 of 95 sera—34·8%—gave a positive complement-fixation test. 23 of these pigeons were examined for the presence of psittacosis virus, 1 by the examination of droppings only; positive results were obtained in 5.

[For part 5, see this *Bulletin*, 1959, v. 34, 92.]

S. P. Bedson

WILKENS, G. L., VAN BAAR, J. & GISPEN, R. Encephalomyelitis bij een geval van ornithosis. [**Encephalomyelitis in a Case of Ornithosis**] *Nederl. Tijdschr. v. Geneesk.* 1958, Apr. 26, v. 102, No. 17, 809–11. English summary.

A description is given of a case of ornithosis complicated by encephalomyelitis. The patient was a man aged 45 who was a bird fancier. He developed an acute illness with pyrexia and severe headache, and after 1 week was admitted to hospital in a typhoid state with rigors, epistaxis and incontinence of urine. The left half of the thorax showed reduced respiratory movement, and infiltration was observed on X-ray examination. A virus of ornithosis type was isolated from sputum taken on the 10th day of illness by the intraperitoneal inoculation of mice and subsequent yolk sac passage. Serum taken at the same time contained complement-fixing antibody to ornithosis group antigen in a titre of 16, and in a further sample taken on the 25th day of illness the titre had risen to 256. The patient recovered after treatment with penicillin. Neurological examination revealed clouding of consciousness with disorientation in time and space, patches of amnesia, confabulation, euphoria, dysarthria, papilloedema, anisocoria and neck rigidity. After the temperature returned to normal the neurological signs disappeared, except for dysarthria and anisocoria, which persisted for a long time. *D. J. Bauer*

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

INST. PASTEUR: SOC. FRANÇAISE DE MYCOL. MÉD. Mycologie Médicale. Communications et rapports présentés aux Journées de Mycologie Médicale (14–15 décembre 1956) organisées par l'Institut Pasteur et la Société Française de Mycologie Médicale. [**Medical Mycology. Communications and Reviews presented at the Conference of Medical Mycology (14–15 December 1956) organized by the Pasteur Institute and the French Society for Medical Mycology**] 344 pp., numerous illustrations. 1958. Paris-VIe: L'Expansion Scientifique Française, 15, rue Saint-Benoît. [3,000 Fr.]

An unsuspecting reader might well suppose that the 34 papers by 73 authors in this quarto volume are hitherto unpublished. This, however, is not the case. Most of the papers have been published before and already have complex histories in print. One on histoplasmosis, to take a random example, first appeared with its coloured plate in *Semaine des Hôpit. de Paris* in February 1957; the next month an independent summary appeared in the *Presse Médicale*, in July there was a fuller version under a variant title in *Arch. Biol. Méd. de Paris* and it is this which again appears, without comment but with the type reset. Other papers have even more complicated histories, and in one instance the printing of some not very informative illustrations one way up in one version and the other way up in another seems hardly necessary. In spite of a state of affairs which ensures bibliographical confusion, this volume is a convenient record of an important series of papers and indicates the flourishing state of the recently formed French Society for Medical Mycology.

The papers are arranged in 6 series: on pulmonary aspergillosis (pp. 11–56), infections of the central nervous system (including cryptoccosis), (pp. 57–90),

moniliasis (pp. 91–205), dermatomycoses (surveys of the incidence of ringworm in different regions of France and the French Cameroons) (pp. 213–29), tropical mycoses (including mycetoma, chromoblastomycosis and rhinosporidiosis) (pp. 239–304), and therapy of mycoses (pp. 309–38). Each paper has summaries in French, German, English and Spanish. On the whole the papers are well illustrated and well documented and all are of good standard. Although it is somewhat invidious to notice individual papers, those by F. MARIAT, *Sur le diagnostic mycologique des principales mycoses du système nerveux central* (pp. 70–86), E. DROUHET and Monique VIEU, *Biologie des infections à "Candida"*, *I* (pp. 115–33) and *II* (by E. Drouhet) (pp. 134–54), *Antifongiques et thérapeutique des mycoses* (pp. 309–32) by E. Drouhet are particularly useful. [Summaries of all the papers appear in *Presse Médicale*, 1957, v. 65, No. 22, 501–3.] *G. C. Ainsworth*

WALKER, Jacqueline. **Survey of the Medical Mycological Literature of Great Britain 1946 to 1956.** *Mycopathologia.* The Hague. 1958, Sept. 29, v. 9, No. 4, 307–340. [Numerous refs.]

This review draws attention to the "striking awakening of interest in the fungus diseases of man and animals" in a country where "grave and fatal types of mycoses are uncommon". The general scope of the survey is indicated by the main topics treated. They include dermatophytoses (pp. 307–17) candidiasis (pp. 317–20) and cryptococcosis (pp. 321–2) which is "endemic in Britain and commoner than the published records indicate", as is aspergillosis (pp. 323–24). Histoplasmosis, which is not considered to be endemic, actinomycosis and mycoses of animals are also covered. *G. C. Ainsworth*

GRIN, E. I. & OZEGOVIC, L. **Critical Survey of Mycological Research and Literature in Yugoslavia up to 1957.** *Mycopathologia.* The Hague. 1958, Sept. 29, v. 9, No. 4, 341–64, 1 fig. + 1 map. [151 refs.]

All but the final 2 pages of this useful and well documented review deal with dermatophytoses in a predominantly rural country where favus (mostly caused by *Trichophyton violaceum*) and infections contracted from cattle are major problems. *G. C. Ainsworth*

EMMONS, C. W. **Association of Bats with Histoplasmosis.** *Pub. Health Rep.* Wash. 1958, July, v. 73, No. 7, 590–95, 1 fig. [16 refs.]

The association of histoplasmosis with bat-infested caves has been well established [CAMPINS *et al.*, this *Bulletin*, 1956, v. 31, 153; MURRAY *et al.*, *ibid.*, 1957, v. 32, 664]. The present outbreak affecting several members of a family is of particular interest in that it occurred in a rural house in Maryland infested with the North American house bat (*Eptesicus fuscus*). Large quantities of bat dung were found in the attic and on the ground at the base of the house and *Histoplasma capsulatum* was constantly isolated from soil samples over a period of 1 year. From a total of 105 soil samples examined, 50 yielded the fungus. The highest proportion of positive samples was obtained adjacent to or within 5 feet of the base of the house.

Although *H. capsulatum* was not isolated from any of 16 bats caught on the premises, the evidence suggested strongly that the saprophytic existence of *H. capsulatum* in the soil was related to the presence of bat dung. As *E. fuscus* is also a common urban dweller, particularly in old houses, it affords a possible explanation for some of the hitherto undetermined sources of histoplasmosis. *Jacqueline Walker*

FROM, P. & ALLI, J. H. **Clinical, Bacteriological and Mycological Evaluation of Tetracycline-Nystatin (Mysteclin) in Pulmonary Disease.** *Antibiotic Med.* New York. 1958, Nov., v. 5, No. 11, 639–48. [18 refs.]

There is some evidence that monilial infections in recent years have increased in virulence and invasiveness. Cultural experiments have proved that the addition to media of penicillin, streptomycin and the tetracyclines greatly enhances mycotic growth. The discovery by HAZEN and BROWN in 1951 [this *Bulletin*, 1951, v. 26, 643] of an antifungal agent within the cells of the soil actinomycete, *Streptomyces noursei*, however, gave promise of a method of control of fungal infections in man. The purified antifungal agent, named fungicidin, later nystatin, proved highly fungicidal and fungistatic, but did not influence bacterial growth. Since the long term treatment of bacterial infections with broad-spectrum antibiotics is frequently complicated by invasion with *Candida* species, the combined use of nystatin with such agents is suggested. In mouse experiments it has already been shown that a single parenteral dose of nystatin, 2 hours before, or at the time of, administration of a potentially lethal injection of *Candida albicans* with chlortetracycline, was definitely protective.

The authors have sought proof of a similar protective action of nystatin in human subjects suffering from chronic pulmonary infections who were to receive a prolonged course of tetracycline (achromycin). The 15 patients in their trial group were all males, aged 37–74 years. An initial investigation comprised a detailed study of the fungal and bacterial flora of the sputum, culture of the faeces for yeasts and staphylococci and culture, for yeasts only, of swabs taken from the alveolar margin and the pharynx, and of the urine.

Treatment comprised a daily oral dose of 1 gm. of a tetracycline-nystatin combination for 10 days, then 0·5 gm. for 20 days. The preparation used was Mysteclin, manufactured by E. R. SQUIBB & Sons [the proportionate composition of which is not stated]. On the 10th and 35th days cultural examinations for *Candida* and staphylococci only were repeated from all sites. The following results were obtained on 10th day. 1 patient who had previously shown *Candida* in the faeces now carried this organism in the mouth and throat, though it was no longer present in the stools. The stools in fact were now free from *Candida* in every patient, though positive cultures had been obtained prior to treatment in 5 instances. The sputum, previously positive in 2 patients, was now free from

Candida in every case. The urine specimens remained free from *Candida*. Regarding the presence of haemolytic coagulase-positive staphylococci in the stools, 2 out of the 3 original carriers still showed this infection and fresh isolations were made from 4 more patients.

On the 35th day (5 days after completion of therapy), 2 patients who had previously carried *C. parakrusei* in the sputum had lost their infection, but 2 fresh infections with *Candida* had arisen. Culture of the gums and pharynx revealed *Candida* in 2 patients, both of whom were passing the organism in their stools. The urine cultures remained negative. Regarding infection of the faeces with pathogenic staphylococci, specimens from 7 patients were now positive, namely the 3 original carriers, 2 out of 4 fresh examples discovered on 10th day and 2 further fresh instances.

The experiment is considered to have shown satisfactory though incomplete control of *Candida* infections during 30 days tetracycline therapy [though the result would have been more informative had it been contrasted with a control group from the same population treated with tetracycline alone]. *J. H. Walters*

JENSEN, K. Ø. Cryptococcosis. Oversigt og et pulmonalt tilfaelde. [**Cryptococcosis. A Survey and a Report of a Case with Pulmonary Involvement**] *Nordisk Med.* 1958, Nov. 27, v. 60, No. 48, 1722–5, 8 figs.

The English summary appended to the paper is as follows:—

"A brief review of the literature on cryptococcosis is presented, followed by a report on a case of primary pulmonary cryptococcosis in a 28 year old farmer, who developed a secondary thoracal fistula from which culture of several samples yielded growth of cryptococci.

"Nine months after the onset of the disease—initially pleurisy of the left lung and mottling of both lungs, later a tumour-like toruloma at the left border of the heart—the patient had completely recovered and was again working as a farmer.

"Recovery seemed to be due to a spontaneous remission rather than to the treatment, which consisted of penicillin, penicillin combined with terramycin, aureomycin, achromycin and potassium iodine.

"The recovered cryptococci showed some minor cultural dissimilarities when compared with known American strains and a Swedish strain of Cryptococcus neoformans.

"The reported case represents the first case of pulmonary cryptococcosis in Denmark, and previously only one case of cerebral cryptococcosis has been reported from this country. This is the fifth case of cryptococcosis reported in Scandinavia.

"The author emphasizes the possibility of a future increase in the number of mycotic diseases, cautions against the indiscriminate use of broad-spectrum antibiotics and recommends cultivation and inoculation in all cases in which the diagnosis is difficult."

GANTZ, J. A., NUETZEL, J. A. & KELLER, L. B. **Cryptococcal Meningitis treated with Amphotericin B.** *Arch. Intern. Med.* 1958, Nov., v. 102, No. 5, 795–800, 6 figs. [23 refs.]

"A case of cryptococcal meningitis treated with amphotericin B ended fatally despite clearing of the spinal fluid of organisms.

"Cryptococcal dermatitis, recurring after excision and sulpfadiazine-iodide therapy, healed completely after seven days' therapy with amphotericin.

"Loss of pathogenicity and reproductive capacity of cryptococci was demonstrated after amphotericin therapy.

"Toxicity to amphotericin was negligible in this patient."

BIDDLE, A. & KOENIG, H. **An Agent effective against Cryptococcosis of the Central Nervous System.** *Arch. Intern. Med.* 1958, Nov., v. 102, No. 5, 801–5. [12 refs.]

"Two cases of cryptococcal meningoencephalitis have been successfully treated with a new antibiotic. One 34-year-old man with a one-and-one-half-year history of central nervous system cryptococcosis was at the point of death in spite of five weeks of treatment with cycloheximide (Actidione). Treatment with a new antifungal agent, amphotericin B, produced remarkable clinical improvement. When the drug was withdrawn after six months of oral therapy, evidence of recurrence of infection was observed. Seven months after a second six-month course of treatment by the intravenous route was concluded, there is no evidence of recurrence. A second 34-year-old man, with a 10-year history of Hodgkin's disease, developed symptoms of central nervous system cryptococcosis. Oral amphotericin B therapy was started six weeks after onset of symptoms, but after seven weeks of treatment symptoms and laboratory data indicated progression. Two months of intravenous administration produced complete remission, which persisted at the last examination, seven and one-half months after treatment was stopped.

"Spinal fluid cultures, drawn seven months and seven and one-half months, respectively, after treatment was stopped, were sterile after one month's incubation, and spinal fluid sugar and cell count were normal at these times.

"At this date we have confirmed arrest in two cases. Longer follow-up periods will be necessary to establish cures. We can recommend, however, the continued use of this drug in an otherwise fatal disease."

KUDEJKO, J. Leczenie promienicy nikozydem na podstawie materiału Kliniki Dermatologicznej Akademii Medycznej w Lublinie zebranego w latach 1953–1955. [**Treatment of Actinomycosis with Nicoside, on the Strength of the Material collected in the Clinic of Skin Diseases, Medical Academy in Lublin, in the Years 1953–1955**] *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1957, v. 12, 267–75. [14 refs.]

The English summary appended to the paper is as follows:—

"The author gives the results of treatment of actinomycosis obtained in 20 patients hospitalized at the Clinic of Skin Diseases, Medical Academy in Lublin, in the years 1953—1955. The treatment consisted in administering nicoside orally in doses of 300—

600 mg daily, as well as topically in injections and by means of iontophoresis. The author presents his own method of topical treatment, consisting in injecting the preparation intrafocally before iontophoresis has been started. Total amount of the administered drug varied considerably, from 9.3 to 108.7 g.

"As far as side-effects are concerned, some patients had slight subjective complaints; 4 elderly patients developed pains in joints after 2—4 months of treatment and in two of them the symptoms produced the picture of periarthritis scapulo-humeralis.

"Out of 14 patients who finished the treatment, 11 were cured in 1 to 5 months, and one patient needed a much more prolonged administration of nicoside (11 months). In 2 patients mentioned above who developed the symptoms of periarthritis scapulo-humeralis, the treatment gave no effect. 6 patients are still under treatment. So far, in all of them a favourable influence of the drug can be observed; 3 approach the clinical healing, the condition of the remaining 3 is much better."

PIMENTEL, J. C. Aspergilose pulmonar de forma tumoriforme ("Aspergiloma pulmonar"). Estudo anátomo-patológico de quatro casos e discussão da sua patogenia. **[Anatomo-Pathological Study of 4 Cases of the Tumour-like Form of Pulmonary Aspergillosis]** *Gaz. Méd. Portuguesa.* 1958, July–Aug., v. 11, No. 4, 455–72, 36 figs. [22 refs.]

The English summary appended to the paper is as follows:—

"The macro and microscopic morphological aspects observed in 4 cases of 'pulmonary aspergilloma' are described and duly interpreted. The A. based on such aspects, the majority of which have not yet been referred to in the bibliography, establishes several evolutive phases of this type of aspergillosis: I—Presence of the aspergillar mass within a pre-existent cavity (illust. 10, 11 and 12); II—Atrophy and erosion of the epithelium at the level of the regions where a close contact of the fungus mass with the wall of the cavity exists (illust. 23, 24 and 25); III—Formation of a granulation tissue at the level of the epithelium deprived areas and its development into the cavity under the form of orange quarters (illust. 26); IV—The filling up more or less extensive of the cavity lumen by the granulation tissue which covers gradually the intracavitary micellar mass and divides it into smaller portions (illust. 28, 29 and 30); V—Production of foreign body giant cells which are perfectly adapted to the contour of the micellar cells divided by the tissue in question (illust. 31, 32, 33 and 34); VI—Re-absorption and removing of the micellar masses.

"In view of these facts, the A. contradicting the opinion of some, does not consider the aspergillus as harmless but on the other hand he does not also admit its invading properties. Nevertheless, its presence in the pulmonary cavity where it is located originates a pathologic process which is primary similar to the one caused by an intrabronchial body. Such processes will have, however, a tendency towards the progressive evolution as it is impossible to remove every foreign body, due to its size and constant growth and still due to the frequency with which processes of secondary infection are associated."

Cancer

LANCASTER, H. O. **Cancer Statistics in Australia.** Part I. *Med. J. Australia.* 1958, Sept. 13, v. 2, No. 11, 350–56, 7 figs. [44 refs.]

The author has made an exhaustive search of the literature concerning Australian cancer statistics and brings into this paper a brief account of the most informative earlier studies. The age-specific mortality rates in Australia from all cancer in the years 1908–55 have shown some improvement in the younger age-groups, at ages 35–64 years in women and at 35–54 in men. At higher ages there has been some increase but part of this may well be spurious, particularly at 75 years and above. Taking a longer period it seems that the cancer death rates up to age 45 have been fairly stable from as long ago as 1870, that over 45 there was a tendency to increase up till about 1930 but that since then there has been a fall in mortality except in the very old.

In a discussion of some individual sites of cancer (in the breast and genito-urinary system) it is noted that cancer of the breast in women was rising up till 1940, since when it has been stationary. Cancer of the uterus has been falling steadily since 1908 especially at ages under 65. There was a marked rise before 1940 in mortality from cancer of the ovary which seems to have ended; the same trend is apparent in cancer of the prostate at ages under 75. Cancer of the testis shows an unusual age distribution with a peak at ages 25–34 years. Cancer of the kidney and bladder has increased somewhat in both sexes.

It is suggested that a cancer registry in each State is necessary to assess the efficiency of treatment and to promote epidemiological and clinical studies.

A. Bradford Hill

NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS. **Carcinoma of the Lung—an NAPT Symposium. Report of a Meeting held in London, 22nd November 1957,** under the Chairmanship of N. L. RUSBY. 48 pp., 6 figs. 1958. London: Tavistock House North, Tavistock Square, W.C.I. [6s.]

This symposium is the report of a meeting held in London on 22 November 1957. It is very short and it

contains economically worded papers on pathology, diagnosis, clinical features, treatment and after-care, but the 2 papers which most concern readers of this *Bulletin* are one by A. Bradford HILL on aetiology and one by K. M. A. PERRY on industry and lung cancer.

Hill briefly restates the evidence on which the opinion has been based that of all the aetiological agents cigarette smoking seems to be the most important—more so than atmospheric pollution.

Perry reviews evidence which indicates that industries in which arsenic (for instance in the sheep-dip industry), chromium compounds and asbestos are used are particularly associated with cancer of the lung. This also is a brief statement of facts already known.

Charles Wilcocks

See also p. 241, DOLL, **Cancer of the Lung and Nose in Nickel Workers.**

See also p. 242, MORGAN, **Some Observations on the Incidence of Respiratory Cancer in Nickel Workers.**

HOFFMAN, H. E. & GRIFFIN, A. C. **Action of Cigarette Tar and Smoke on Chemically Induced Carcinogenesis.** *Texas Reports on Biol. & Med.* 1958, v. 16, No. 3, 333–45. [30 refs.]

Carcinogens have sometimes been found to inhibit the effect of other carcinogenic agents. In particular it has been found that methylcholanthrene will inhibit the production of hepatic cancers by 2-diacetylaminofluorene (DAF). Experiments were, therefore, made to see whether any such effect would be produced by cigarette smoke or tar. Groups of rats were fed semi-synthetic diets containing 0·05% DAF for 2 to 3 months; some groups were exposed to various amounts of cigarette smoke blown into their boxes and other animals were injected intraperitoneally with a preparation of crude tobacco tar. The treated groups showed less damage to the liver and a smaller reduction of hepatic riboflavin than the control groups. Similar injections given to rats fed 0·06% 3′-methyl-4-dimethylaminoazobenzene failed to affect the reduction in liver riboflavin, but the amount of liver damage was again grossly inhibited.

Richard Doll

BAILEY, Esmé J. & DUNGAL, N. **Polycyclic Hydrocarbons in Icelandic smoked Food.** *Brit. J. Cancer.* 1958, Sept., v. 12, No. 3, 348–50.

"(1) 3 : 4 Benzpyrene has been detected and estimated in smoked mutton, trout and red fish.

"(2) The smoked mutton and trout, which had been smoked on the farms contained a higher proportion of all polycyclic hydrocarbons.

"(3) The amount of 3 : 4 benzpyrene detected in 1000 g. smoked trout and mutton was comparable with the amount of 3 : 4 benzpyrene in the mainstream smoke from 250 cigarettes (Gilbert and Lindsey, 1956)."

COMMINS, B. T. & LAWTHER, P. J. **Volatility of 3,4-Benzpyrene in relation to the Collection of Smoke Samples.** *Brit. J. Cancer.* 1958, Sept., v. 12, No. 3, 351–4, 1 fig.

"Experiments have failed to show the presence of vapour of 3,4-benzpyrene in town air.

"No appreciable volatilisation of 3,4-benzpyrene occurs at room temperature when air is passed at rates of 1 cu. m./minute through impregnated filters for 2 hours. Nor is there any detectable loss of the hydrocarbon after aspiration of air at rates of 0·3 litres/minute through impregnated sintered discs for 17 hours.

"Appreciable losses occur at 100°C. even at flow rates of 0·3 litres/minute and at temperatures of 170–200°C. the loss is complete after 5 minutes treatment.

"The relevance of these findings to sampling techniques is discussed."

Miscellaneous Diseases

DEVADATTA, S. & VERGHESE, S. **Chronic Lead Poisoning.** *J. Indian Med. Ass.* 1958, Oct. 16, v. 31, No. 8, 328–30.

In this paper there is an account of 4 cases of chronic lead poisoning in 4 adults from 2 Brahmin families which are believed to have been caused by the use of lead vessels for the preparation and storage of curds. Among the symptoms and signs in these patients were progressive weakness of the extensors resulting in bilateral wrist drop and abdominal pains of colicky type. Convulsions occurred in 2 patients, 1 of whom died. No lead analysis of blood or urine were carried out but coproporphyrin III was found in the urine and there was basophilic stippling of red cells. There was a blue line on the gums in all 4 patients.

It is believed that chronic household lead poisoning may be much more frequent in South India than is generally supposed because the patients stated that a number of families in the locality were using leaden vessels.

M. E. Delafield

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order : General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

HOPWOOD, B. E. C. **The Place of Industrial Medicine in Uganda.** *Internat. Labour Rev.* 1958, Oct., v. 78, No. 4, 348–67.

The economic life of Uganda depends chiefly on agricultural products produced by a peasant labour force. By 1957 only 310,000 out of a population of over 5½ millions worked for others. The majority of the unskilled workers have had no schooling and work only to achieve a particular target—enough money for a bicycle or a bride or a wireless set. Among the more permanent skilled class early retirement between 45 and 50 is general.

Some 50,000 are employed, raising plantation crops—coffee, tobacco, sugar, tea, rubber and sisal, and there are secondary industries producing these crops—cotton seed into oil and soap, tobacco into cigarettes, sugar refining and so on. There are a large number of sawmills and building and construction work is one of the largest industries. Some 5,000–7,000 are employed in mining and quarrying and there is a wide range of small plants keeping the larger towns supplied and serviced—engineering and repair shops, food and drink factories, manufacturers of clothing, furniture and leather goods, printing works and small foundries. Most of this industrial development has taken place in the last 20 or 30 years.

A difficult and distinctive problem in maintaining the health of the labour force is that much of it migrates long distances to seek employment. Legislation at the factory site follows patterns common elsewhere in the world, but the migrant often finds himself faced with diseases strange to his home environment, particularly schistosomiasis, onchocerciasis and different forms of malaria.

The law compels those recruiting labour to provide transport, food and medical care on the migratory journey, and medical supervision and in certain cases housing for those who live on the working premises—a minimum food scale is also laid down for recruited labour.

The actual industrial hazards are much the same as those found in similar industries elsewhere. The handling of pesticides and weed killers is a prominent one. Where toxic agents that vaporize are handled there is increased danger on account of high temperatures and humidity. There is an erroneous assumption common among some employers that the African can withstand deficient ventilation conditions better than others.

The task of education in matters of industrial hygiene and safe working practices is particularly difficult on account of language difficulties and the frequent absence of even elementary schooling.

T. O. Garland

FRANKE, W. Der Feuerstar in messtechnischer Beziehung und gewerbehygienischer Bedeutung. [**Radiation Cataract: Scientific Measurement of Conditions of Work and their Hygienic Importance**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 539–54, 4 figs. [18 refs.]

Cataract has been known for decades as an industrial disease of glass blowers and was added to the list of industrial diseases entitling to compensation in Germany in 1925. Descriptions of lens opacities in workers in industries in which there was exposure to the radiation from molten materials other than glass were also published especially in England. In this paper reference is made to studies on the frequency of cataract in glass blowers as compared with that found in men working in smelting, rolling mills and iron works. The incidence of lens opacities is highest in the glass blowers.

The purpose of the work described in this paper was to measure as accurately as possible the physical conditions of infra-red radiation and temperature to which workers are exposed in the various industries in which cataract appears as an occupational risk. It is realized that constitutional and factors other than physical conditions may play a part in the onset of cataract. Infra-red radiation was measured by means of an instrument which is fully described with a photograph, and its scientific use is discussed. Measurements with this instrument were made in a number of steel and light metal works, a glass factory and also of sources of infra-red radiation used for technical purposes in other industries. The results are set out in a long table which gives particulars of the place where the measurements were made, the temperature of the source of radiation, the distance away from this source and the amount of infra-red energy received by the eye. In addition a number of glass and metal workers were examined ophthalmologically by the slit lamp. The measurements obtained are discussed at length. The highest infra-red figures were found in a steel works. These were 3–4 times greater than those in the glass works. Nevertheless the measurements confirm the view that the radiation hazard is less in the metal industry than in the glass industry for the reasons that in metal workers the period of exposure is shorter, the distance from the source of radiation is greater and protective measures can more readily be applied.

M. E. Delafield

MOLFINO, F. & ODAGLIA, G. Risultati e rilievi in tema di decompressione terapeutica nelle malattie barotraumatiche. [**Results and Observations on Decompression Treatment of Barotraumatic Diseases**] *Med. d. Lavoro.* 1958, Oct., v. 49, No. 10, 565–71. 3 figs. [10 refs.]

The English summary appended to the paper is as follows:—

"A short description is given of the apparatus used at the Institute of Industrial Medicine of the University of Genoa at S. Martino's Hospital (large fixed chamber for multiple simultaneous decompressions and single mobile rigid and telescopic chambers) and the activity of this Center is outlined. The techniques used for decompression treatment are briefly described. Observations on treated cases are then reported with regard to ECG changes (during treatment patients are continuously controlled by ECG) and final therapeutic results. The importance of a rational and correct treatment method in obtaining the best results is pointed out."

NATIONAL COAL BOARD. **Annual Report and Accounts for the Year ended 28th December, 1957** [BOWMAN, J., Chairman]. Volume I: Report. pp. vii + 64, 1 map. 1958. London: H.M. Stationery Office. [4s.]

By the end of 1957 there were 344 collieries of 800 men or more at which a medical centre in the charge of a registered nurse was employed, and there remain 65 centres still to be completed; at smaller pits there are medical rooms staffed by medical room attendants. Arrangements have now been made for all entrants to the industry to be examined radiologically; in 1957 80 doctors were employed by the Board.

For pneumoconiosis the number of certifications fell on the whole in 1957, but increased in 3 Divisions; this, however, is not a reflection of any increase in incidence, but of the fact that there is greater awareness of the disease among mine workers, and the X-ray facilities are better. The main project of medical research was the field work which involves regular X-ray examination of 35,000 miners and collection of records of dust in the pits in which they work. A test of respiratory function is carried out on these men.

The "beat" affections remain intractable but a new knee pad is being tried. Fungicidal foot sprays are installed in some pit-head baths in an attempt to control athlete's foot.

The cost of research on medical and allied problems in 1957 was £144,000. *Charles Wilcocks*

CENTRAL MINING-RAND MINES GROUP. HEALTH DEPARTMENT. **Report for the Year 1957** [COETZEE, A. M., Chief Medical Officer]. 26 pp., 2 folding charts. 1958. Johannesburg: P.O. Box 1056.

This report follows the form of the long series of its predecessors, and it opens with a tribute to Dr. A. J. ORENSTEIN, who resigned during the year from the post of Chief Medical Officer which he had held with distinction for 42 years, and who has now been appointed Director of the Pneumoconiosis Research Unit of the South African Council for Scientific and Industrial Research.

A large increase is reported in the incidence of disease in the 78,736 workmen, but this is almost accounted for by the large number labelled as "influenza" during the epidemic. Accidents due to employment remain about the same at 270 per 1,000 with a mortality of 1·63 per 1,000. The pneumonia rate at 36·95 per 1,000 shows little difference from the rate in 1947, but the case mortality at 0·89% has been halved in that time.

The pulmonary tuberculosis morbidity rate was 11·78 per 1,000 in 1915, and 3·26 in 1957; the mortality rates were 1·48 and 0·14 per 1,000 respectively. Silicosis was diagnosed in 112 cases (1·42 per 1,000), and with the arrival of the necessary X-ray apparatus at the mines a start was made to comply with the requirements of the Pneumoconiosis Act by making bi-annual radiological examinations.

Hospital costs have risen slightly since 1954, but feeding costs (foodstuffs only) in the mines as a whole were £21.9.7. per annum (against £5.7.2. in 1933 and £13.8.2. in 1947) for each African.

Charles Wilcocks

MEIKLEJOHN, A. [M.D.] **The Life, Work and Times of Charles Turner Thackrah, Surgeon and Apothecary of Leeds** (1795–1833), pp. vii + 238, 7 figs. on 7 pls. 1957. Edinburgh. London: E. & S. Livingstone Ltd. [25s.]

[This book was reviewed on p. 184.]

ATTINGER, E. O., GOLDSTEIN, M. M. & SEGAL, M. S. **The Mechanics of Breathing in Normal Subjects and in Patients with Cardiopulmonary Disease.** *Ann. Intern. Med.* 1958, June, v. 48, No. 6, 1269–88, 3 figs. [40 refs.]

Pulmonary compliance (elastic resistance), mechanical resistance (flow resistive pressure), vital capacity and maximum breathing capacity were measured in 100 persons of whom 25 were normal and 75 had various types of cardiopulmonary disease.

In normal subjects compliance was independent of respiratory rate as long as the respiratory mid-position was constant. Inspiratory and expiratory mechanical resistance did not differ significantly.

Pulmonary disease. Compliance was lower than normal except in emphysema. (It is difficult to measure true static pressure in dyspnoeic emphysematous patients, and flow-dependent values were obtained which were within normal range.) Mechanical resistance was higher than normal. Expiratory resistance was considerably higher than inspiratory resistance.

Cardiac disease. These patients showed a lower compliance and higher mechanical resistance than normal. Although expiratory resistance was higher than inspiratory resistance, the difference between the two was less than in bronchospastic subjects.

During remission asthmatic subjects might have compliance and mechanical resistance within normal range. The correlation between vital capacity and compliance was good in all diseases except emphysema. Restrictive lung disease and pulmonary fibrosis had a low and stable compliance and a somewhat increased mechanical resistance, resembling cardiac disabilities in this respect. *M. L. Thomson*

RAVIN, H. A. & STEIN, M. **Bedside Measurement of Alveolar Carbon Dioxide Tension.** *New England J. of Med.* 1958, Oct. 23, v. 259, No. 17, 811–13, 5 figs.

A sample of alveolar gas is trapped in a lucite (perspex) chamber of 50 to 100 ml. capacity. The CO_2 is absorbed by caustic soda solution and the resulting fall in pressure, which is equal to the partial pressure of CO_2, is read on an anaeroid gauge connected to the chamber. The caustic soda solution is contained in a sealed glass phial which is shattered by vigorous shaking against a steel bar inside the chamber. To wash out the lung-dead-space 750 ml. expired air are required and 300 to 600 ml. to wash out the chamber; thus the sample should only be collected after 1,050 to 1,350 ml. have been expired. *M. L. Thomson*

MCGREGOR, M., with the technical assistance of Lilian MALKIN, Meryl LENNOX & Jeanette O'DONOVAN. **The Value of an Index of Maximal Expiratory Force in the Interpretation of Tests of Maximal Ventilatory Capacity.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 692–6.

It is sometimes forgotten that indices of ventilatory capacity such as maximal breathing capacity and maximal mid-expiratory flow rate depend on the power of the chest bellows as well as on airway resistance. In addition to these 2 tests maximal expiratory pressure and expiratory resistance (by oesophageal catheter and pneumotachograph) were performed on 99 miners who varied in health from normal to advanced obliterative pulmonary disease. It was hoped that the maximum expiratory pressure would enable chest muscular power to be assessed independently of airway resistance which itself could be measured by oesophageal catheter.

The highest correlation (r = 0·59) was found between the ventilatory tests and the ratio of maximum expiratory pressure to resistance. The best estimate was thus obtained from the regression equation: resistance = maximum expiratory pressure/0·145 maximum breathing capacity + 4·36.

M. L. Thomson

SARTORELLI, E., GRIECO, A. & TOMASINI, M. Studio dell'elasticità polmonare negli enfisematosi mediante la determinazione della curva delle pressioni di rilassamento. **[Study on Pulmonary Elasticity in Emphysematous Patients by determining the Curve of Relaxation Pressure]** *Med. d. Lavoro.* 1958, Oct., v. 49, No. 10, 591–7, 4 figs. [13 refs.]

The English summary appended to the paper is as follows:—

"The behaviour of pulmonary elasticity in emphysematous patients was studied by setting up the curve of chest and lung relaxation pressure, according to Rahn et al.; this curve makes it possible to calculate the relaxation volume and the elastic work on breathing. 32 emphysematous male patients were examined: 20 of them had a moderate degree of emphysema (average age: 51.3 years) and 12 an advanced emphysema (average age 52.4 years). As controls, the results obtained in a previous study in a group of normal male subjects (average age: 44.6 years) are reported. In the two emphysematous groups the average value of relaxation volume was found to be respectively 46.4% and 53.9% of the vital capacity (there is a statistically significant difference between normal value, i.e. 40.3% of the vital capacity and the values of both emphysematous groups, as well as between the values of the two groups); the average value of maximum expiratory relaxation pressure was found to be respectively 12.5 mmHg and 6.2 mmHg (statistically significant difference between the normal average value, 22.3 mmHg, and the values of both emphysematous groups, as well as between the values of the two groups); the average value of elastic work on breathing, corresponding to a ventilatory volume of 500 ml, was found to be respectively 847 g. cm and 625 g. cm (statistically significant difference between normal average value, 981 g. cm, and the average value of the severe emphysema group).

"The results obtained show that there is an average decrease of pulmonary elasticity in emphysematous patients, and that the more severe the emphysema the greater is this decrease."

SARTORELLI, E. & GRIECO, A. Spazio morto respiratorio e ventilazione alveolare negli enfisematosi e nei silicotici. **[Respiratory Dead Space and Alveolar Ventilation in Emphysematous and Silicotic Patients]** *Med. d. Lavoro.* 1958, Oct., v. 49, No. 10, 598–609, 7 figs. [18 refs.]

The English summary appended to the paper is as follows:—

"The behaviour of the respiratory dead space (D.S.) has been studied in several groups of emphysematous and silicotic patients, by means of a D.S. measuring method, in which maximal alveolar CO_2 concentration is used for calculating Bohr's formula. Alveolar CO_2 concentration URAS-M is obtained from CO_2 expiratory curve registered by infrared gas analyses.

"By substracting D.S. ventilation values from pulmonary ventilation, alveolar ventilation values were obtained and thereby it was possible to calculate the alveolar ventilation $\times$ 100 / Pulmonary ventilation ratio, index of ventilatory efficiency.

"The following results were obtained. Two groups of emphysematous male patients, one of 6 subjects with slight emphysema (average age 49.7 years) and the other of 8 subjects with advanced emphysema (average age 49.4 years), had respectively the following D.S. average values: 165 ± 35 ml and 247 ±55 ml. The difference between the two groups is statistically significant (P = 1%).

"Three groups of male silicotic patients, the first of 8 subjects with pinhead or micronodular silicosis (average age 51.4 years), the second of 5 subjects with nodular silicosis (average age 46.0 years) and the third of 8 subjects with nodular conglomerated or massive silicosis (average age 56.1 years) had respectively the following D.S. values: 160 ± 43 ml; 182 ± 16 ml; 183 ± 16 ml; the differences between average values in the three groups were not statistically significant.

The comparison of the average D.S. values obtained in the different groups of emphysematous and silicotic patients with the average D.S. values of a group of normal subjects of the same average age (49.7 years) showed statistically significant differences only between advanced emphysema patients and the normal ($P < 0.1\%$) and between massive silicotic patients and the normal ($P = 1\text{-}0.1\%$). The average values of the $\frac{\text{alveolar ventilation} \times 100}{\text{pulmonary ventilation}}$ ratio obtained in the two emphysematous groups (slight and advanced) were respectively 67.8 ± 7.7 and 59.7 ± 4.4; in the three silicotic groups (pinhead or micronodular, nodular and massive) they were respectively 65.4 ± 3.9; 64.5 ± 6.5 and 56.6 ± 7.0. Ventilatory efficiency therefore was found to be in average definitely decreased from the normal values in advanced emphysematous and massive silicotic patients."

[URAS-M is an apparatus for rapid estimation of CO_2 by infra-red rays. See SCHERRER and HODLER, *Schweiz Med. Woch.*, 1957, v. 87, 1509.]

MAGISTRETTI, M., LO MARTIRE, N., PEIRONE, E. & SARTORELLI, E. Studio della commistione venosa polmonare negli enfisematosi, nei silicotici e nei silicotubercolotici. [**Study of Pulmonary Venous Admixture in Emphysematous, Silicotic and Silicotuberculotic Patients**] *Med. d. Lavoro.* 1958, Oct., v. 49, No. 10, 610–20, 2 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The study of arterial O_2 saturation after oxygen administration at intermittent positive pressure (I.P.P.B.) allows a qualitative evaluation of the importance of physiologic venous admixture in the genesis of arterial anoxemia. Physiologic venous admixture, a fraction of total venous admixture, is due to the presence of well perfused but poorly ventilated areas of pulmonar parenchyma: the blood that flows in these areas is only partly involved in gaseous exchanges and therefore cannot be fully saturated with O_2. This fraction of pulmonary flow determines an arterial anoxemia varying according to the amount of alteration of the ventilation/perfusion ratio. The administration of pure oxygen at intermittent positive pressure considerably increases alveolar pO_2 and eliminates the physiologic component of total venous admixture.

"We examined 99 subjects grouped as follows: 15 normal control subjects; 35 subjects with advanced emphysema; 26 silicotic subjects 10 of which had pinhead or micronodular silicosis, 3 had nodular silicosis and 3 had conglomerate nodular or massive silicosis; 23 silicotuberculotic subjects in which a discrete nodular or a conglomerate nodular or massive silicosis was associated with active cavitary tuberculosis with areas of recent exudative infiltration. The study of pure oxygen administration at I.P.P.B. (10 cm H_2O) on O_2 saturation of arterial blood showed that the slight anoxemia of normal subjects is due to physiologic venous admixture. Also in emphysematous subjects such component of the total venous admixture is the predominant element in the genesis of desaturation. In silicotic subjects the behaviour of O_2 saturation in arterial blood during pure O_2 administration was not univocal, showing that the influence of physiologic and respectively anatomic venous admixture in the genesis of anoxemia can vary from case to case. In silicotuberculotic patients, on the contrary, anatomic venous admixture has a particular importance in determining anoxemia, as shown by the fact that it is practically not modified by pure oxygen administration at I.P.P.B."

MAGISTRETTI, M., SARTORELLI, E., BRINA, A. & RUBINI, G. Frequenza della comparsa in lavoro di segni ecgrafici di sovraccarico ventricolare destro nei soggetti normali e nei silicotici. [**Frequency of ECG Signs of Right Ventricle during Work in Normal and Silicotic Patients**] *Med. d. Lavoro.* 1958, Oct., v. 49, No. 10, 621–9, 2 figs. [23 refs.]

The English summary appended to the paper is as follows:—

"Muscular-work, in subjects with chronic pulmonary diseases such as silicosis, often induces an increase of pulmonary vascular resistance and therefore an excessive work of the right ventricle. When the increase of the right ventricle work is higher than its capacities for functional compensation, a right ventricle surcharge appears and can be shown by a typical ECG picture.

"Up to now studies on the frequency of such an ECG picture during muscular work in silicotic patients did not give univocal results. This investigation was therefore performed in order to ascertain whether, in silicotic patients with normal ECG at rest, the ECG signs of right ventricle surcharge during work were higher than in normal subjects.

"Fifty normal male subjects, 20 to 65 years old, and 56 silicotic male patients, 25 to 60 years old, were examined. All normal and silicotic subjects showed a normal ECG at rest. Each subject was submitted to an ECG examination during aerobic muscular work and then during anaerobic work (marching on a treadmill at 15% inclination and various speeds). The following results were obtained: aerobic work did not induce in any subject any pathologic change of the ECG. During anaerobic work a certain number of subjects both normal and silicotic, showed one or more ECG changes corresponding to signs of right ventricular surcharge.

"The statistical analysis of the data, however, showed that there are no significant differences between the normal subjects and patients with silicosis at any stage. This finding is in contrast with the observation that, due to the anatomic and functional changes reducing the elasticity of the pulmonary vascular system, muscular work induces in silicotic patients the appearance of pulmonary hypertension and therefore of the right ventricular functional surcharge more often than in normal subjects. This discrepancy can be justified by the fact that the ECG changes, typical of the right ventricular surcharge, are masked by the 'indirect' changes due to absolute or relative coronary insufficiency of the left ventricle (left ventricular surcharge), which often occur in silicotic patients during intense muscular work.

"The present findings indicate that there is no constant connection between hemodynamic surcharge and appearance of typical ECG signs, and that therefore the use of ECG is very limited as a diagnostic means for evaluating the hemodynamic conditions of the pulmonary circulation in subjects with chronic pulmonary diseases."

WRIGHT, B. M. **A New Nebuliser.** *Lancet.* 1958, July 5, 24–5, 2 figs.

This nebulizer was developed in the Pneumoconiosis Research Unit of the Medical Research Council, Cardiff for use in the wards, in response to a demand for one which was robust and easy to clean. It is made entirely of Perspex and can be used with an oxygen cylinder or on the piped oxygen supply now installed in many hospitals. At a pressure of 20 lb. per square inch it delivers 10 litres of oxygen a minute and nebulizes about 20 ml. of liquid per hour, giving droplets of 1–6 μ diameter at a given gas flow. It can be used for producing therapeutic aerosols or as a humidifier.

Full details are given and illustrated.

Charles Wilcocks

ROACH, S. A. **Counting Errors Due to Overlapping Particles in Thermal Precipitator Samples.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 250–57, 5 figs. [10 refs.]

250 pairs of dust samples were taken in coal mines with adjacent thermal precipitators, 1 of which was operated for 5 times as long as the other. The numbers of particles counted by the longer running instruments were much less than 5 times as many because some particles were deposited in contact and, in accordance with the usual counting convention, such aggregates were taken as single particles on the assumption that aggregation had occurred while the particles were airborne instead of being an instrumental artefact.

Comparison with a previously published theoretical formula for "overlap error" revealed that the correction to the total count, which increases with the number of particles per unit area of sample, was slightly greater than the theoretical prediction. This is ascribed to the fact that the approach of the particles to the sampling plate was oblique and to the variation of density of deposit across the width of the trace.

The common practice of counting only particles in the 1–5 micron size range, out of all those deposited, leads to a considerable magnification of the overlap correction which has not previously been noted.

Overlap errors have undoubtedly led to underestimates of dust concentration, and to overestimation of size.

C. N. Davies

HOFFMANN, A. Staubimmissionsmessungen und ihre statistische Auswertung. [**Measurement of Dust Emission and its Statistical Evaluation**] *Staub.* Düsseldorf. 1958, Nov. 1, v. 18, No. 11, 338–41.

The English summary appended to the paper is as follows:—

"To keep the air free from annoying and injurious substances, there is necessary a methodical observation of the impurifications of the air and this embraces analyses of the air one breathes and of the precipitations of the atmosphere. The evaluation of the results must be undertaken with special methods which permit objective affirmations within certain limits of reliability. The use of mathematical statistics has proved itself suitable for this purpose. The methods of the simple and the multiple dispersion analysis are shown by means of the example of the evaluation of measurings which were taken in a big town in the Ruhr area and the further possibility of application of the statistical methods is indicated."

LUHR, H. G. Quantitative Untersuchungen über die Phagocytose von Kohlenstäuben verschiedenen Inkohlungsgrades sowie Quarz—und Diamantstaub in der Gewebekultur. [**Quantitative Examination of the Phagocytosis of Various Coal Dusts, Quartz Dust and Diamond Dust in Tissue Cultures**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 3, 355–60, 3 figs. [17 refs.]

This paper contains an account of the laboratory investigations which were undertaken to obtain a quantitative picture of the phagocytosis of a number of different dusts by cells in a tissue culture. The experiments are fully described and the findings were tested statistically. Physical and other particulars are given of the pure quartz dust, the different coal dusts and the diamond dust which were used in the experiments. The preparation and constitution of the cultures of lung tissue from 3-day-old mice into which the dusts were introduced are fully described. After incubation for periods of 16–24 hours the tissue cells were examined by phase-contrast microscopy and the dust particles contained in them were enumerated.

The results of these tests are fully discussed. It was found that of every 100 cells an average of 75·3 ± 3·6 cells had taken up dust particles irrespective of the type of dust which had been added. The average number of dust particles seen in 10 cells which had taken in dust after 16 hours of incubation was 118·7 ± 6·3 in the case of the diamond dust but only 59·5 ± 6·0 with quartz dust. The numbers in the case of 2 different types of coal dust were 65·5 ± 14·5 and 70·4 ± 5·3. Some photographs are given of the phagocytosis of dusts by mouse lung cells.

M. E. Delafield

BARHAD, B., PETRESCO, L. & SARF, I. Modifications respiratoires sous l'influence des poussières. [**Respiratory Modifications due to Dust**] *Arch. Malad. Professionnelles.* Paris. 1958, May–June, v. 19, No. 3, 258–64, 6 figs.

In this paper the authors verify experimentally the results of investigations previously carried out in factories [this *Bulletin*, 1957, v. 32, 864]. Volunteers inspired dust from a cabinet (HUHRINA and VORONTZOVA, *Gigiena i Sanitariya*, 1954, v. 11, 20) which provided a constant, controlled dust concentration, through a half

mask equipped with hand-operated sampling port and connexion to a tambour for recording respiratory excursions.

It was found in this way that percentage retention of cement particles around 1 μ in diameter rose from 20 to 70 when the number of particles rose from 500 to 6,000/cm.^{3}. The tidal volume was only 21–60% of that found when air was breathed. The ratio of duration of expiratory to inspiratory phase averaged 2·2 in pure air and increased to 3·2 when dust was breathed.

M. L. Thomson

MORROW, P. E. & GIBB, F. R. **The Deposition of a Submicronic Aerosol in the Respiratory Tract of Dogs.** *Amer. Indust. Hyg. Ass. J.* 1958, June, v. 19, No. 3, 196–200, 7 figs. [15 refs.]

The aerosol consisted of submicronic crystals of sodium chloride; this was contaminated with an alpha ray emitter, ^{210}polonium, which greatly facilitated measurements on the distribution of the aerosol after inhalation. The animals used were bitches ranging in weight from 6 to 12 kgm. The mean deposition value was found to be 66·5% of the aerosol mass respired.

The experiments were part of a fundamental study on the rôle of certain factors in dust deposition (comparable to studies on man).

On the whole the authors conclude that, despite anatomical differences, such as for instance the disproportionately larger nasal pharynx and trachea in the dog, there is a great similarity in the way both dog and man deal with this aerosol when it is taken in to the lungs. Based on the distribution, excretion and lung recovery of the polonium, it is possible to estimate the amount of the aerosol which was deposited in the upper and lower respiratory tract. The whole scheme of experiment is one part of an extensive study of what happens to man after inhaling noxious substances.

S. Russ

MORROW, P. E., MEHRHOF, E., CASARETT, L. J. & MORKEN, D. A. **An Experimental Study of Aerosol Deposition in Human Subjects.** *Arch. Indust. Health.* Chicago. 1958, Oct., v. 18, No. 4, 292–8, 4 figs. [65 refs.]

Human observers inhaled an aerosol containing about one million particles of solid sodium chloride per cc. with a median diameter of 0·052 micron. The percentage mass deposition in the respiratory tract was measured by comparing the concentrations in the inhaled and exhaled clouds and plots are given relating it to the mean respiratory frequency, the mean tidal volume, the mean inspired air flow rate and the mean expired air flow rate. The data were obtained by recording the characteristics of the subject's breathing, which was uncontrolled. An equilibration period of 8 or more minutes was allowed to each subject before making observations which lasted from 5 to 20 minutes.

The results show that the manner in which the subject breathes has a marked effect upon deposition. The average deposition over the whole series was 63·4%.

C. N. Davies

NAGELSCHMIDT, G., NELSON, E. S., KING, E. J., ATTYGALLE, D. & YOGANATHAN, M. **The Recovery of Quartz and other Minerals from the Lungs of Rats. A Study in Experimental Silicosis.** *Arch. Indust. Health.* Chicago. 1957, Sept., v. 16, No. 3, 188–202, 7 figs. [16 refs.]

"In the course of pneumoconiosis research the recovery of a number of dusts injected into rats' lungs was studied by determining the amounts retained in lungs and lymph nodes at different times, up to one year after injection.

"Two experiments with five flint fractions of graded size (below 0.5μ to 8μ), which had been injected at constant surface showed, between 3 and 12 months after injection, constant total recoveries of the order of 55% of the amounts injected for the four larger fractions (0.5μ to 8μ); a lower total recovery of the order of 40% was obtained for the smallest fraction (below 0.5μ).

"Recoveries of highly fibrogenic quartz and of almost inert corundum of equal size were studied in three experiments. Except for the first two months after injection, the total recoveries of both materials were equal, dropping after three months to about 60% and thereafter remaining constant up to one year. The amounts of dust in the lymph glands increased with time, and after one year 28% of the total quartz recovered was in the lymph glands as against 16% of the corundum.

"A comparison of the properties of quartz isolated after different time intervals from the lungs showed that a loss of a small percentage had occurred because of solubility; reasons are given why the dissolution of silica is thought not likely to be the controlling factor in fibrogenesis.

"Recoveries of anthracite and bituminous coal dusts showed no clear difference between the two coals. The total recoveries as a function of time were very similar to those of quartz and corundum; after one year the proportion of dust in the lymph glands was 10%, somewhat lower than for corundum, and considerably lower than for quartz or flint of similar size.

"In two pilot experiments with labeled tantalum carbide and scandium oxide, recoveries were measured by Geiger-Müller counting technique. The results were very different, TaC being rapidly lost from the lungs and Sc_2O_3 only very slowly.

"The gravimetric work which was based on more than 300 analyses showed that all dusts of comparable size gave very similar total recoveries, irrespective of their fibrogenic activity. After a period of rapid loss of dust during the first two months, probably due to removal via the bronchi, there was no further measurable loss, but continued movement of dust from the lungs to the lymph glands took place. Fibrogenic dusts were transported more than inert dusts. With fibrogenic dust (flint) size was important: the smaller the size of the flint, the higher was the proportion that went to the lymph nodes, and the earlier did it get there.

"The bearing of the results on our knowledge of dust retention is discussed."

GLÖMME, J., HOLMQUIST, C. E. & SWENSSON, Å. **Studies on the Toxicity of Silicic Acid.** *Arch. Indust. Health.* Chicago. 1958, Mar., v. 17, No. 3, 204–9, 3 figs. [28 refs.]

"A practically pure silicic acid in supersaturated solution was produced by ion exchange.

"The content of low polymerized AMR (ammonium molybdate reactive) silicic acid was observed during the first days after preparation. The concentration fell rapidly, and after two days was almost equal to the equilibrium concentration.

"The polymerization and formation of CP (colloidal polymerized) silica continued, and gel formation was observed after about two weeks.

"The primarily formed, low molecular silicic acid had a low toxicity; the lethal dose for mouse was 5.4 mg/30 gm. on fractionated injection intravenously.

"As polymerization progressed, the toxicity increased, rapidly at first and then more slowly.

"After 80 days the lethal dose, 0.28 mg/30 gm. mouse, was similar to the toxicity of very fine synthetic amorphous silica (average particle size about 0.010μ), i.e., 0.20 mg/30 gm.

"Addition of hydroxyethylcellulose to delay polymerization gave some immediate rise in toxicity, which was not subsequently increased."

SCHEPERS, G. W. H., DELAHANT, A. B., FEAR, Elizabeth J. & SCHMIDT, J. G. **The Biological Action of Degussa Submicron Amorphous Silica Dust (Dow Corning Silica). IV. Studies on Guinea Pigs infected with Tuberculosis.** *Arch. Indust. Health.* Chicago. 1957, Nov., v. 16, No. 5, 363–79, 4 figs. & 3 pls. [12 refs.]

"A series of 115 guinea pigs were infected by inhalation with the Mycobacterium tuberculosis var., RIRv.

"Of these animals, 48 served as controls. A second group of 41 guinea pigs was exposed to Degussa submicron amorphous silica dust (Dow Corning Silica) for periods up to two years, exposure commencing immediately after infection (simultaneous phase). A third group of 26 guinea pigs was divided into three subgroups, and these subgroups, placed in the dust room at two-, four-, and six-month intervals after infection, were observed for periods up to a year (reactivation phase).

"The inhalation of the Degussa dust transiently stimulated the infective process. This augmentation of the tuberculous response was slight and occurred primarily during the simultaneous phase experiment.

"The tuberculous infection progressively aggravated the pneumoconiotic process during the simultaneous phase experiment so that it attained moderate severity at the end of two years of continuous dust exposure.

"In the reactivation phase experiment both the tuberculous response and the pneumoconiotic reaction were partly inhibited after initial transient stimulation.

"The medicolegal implications of these observations and their relationship to the problem of human silicosis and its tuberculous complication are reviewed.

"Suggestions are made concerning lines of research which should be further pursued to elucidate extant problems."

SCHEPERS, G. W. H., DELAHANT, A. B., BAILEY, D. A., GOCKELER, E. L. & GAY, W. C. **The Biological Action of Degussa Submicron Amorphous Silica Dust (Dow Corning Silica). V. Injection Studies.** *Arch. Indust. Health.* Chicago. 1957, Dec., v. 16, No. 6, 499–513, 3 pls.

"Injection experiments on rats, guinea pigs, and rabbits, using the Degussa submicron amorphous silica dust, are described, the routes explored being the intraperitoneal, intratracheal, and intravenous.

"The intraperitoneal introduction of 200 mg. of dust in guinea pigs caused death. For the majority of the rats the dust also proved lethal when administered intratracheally in a 37.5 mg. dose. Guinea pigs, on the contrary, tolerated an intratracheal dose of 75.0 mg. fairly well. Of five rabbits, three died of doses of 100 mg. to 1,000 mg. of the dust introduced intravenously, while two survived injections of 1,000 mg.

"In rats the main features were diffuse pulmonary granulomata in which necrosis occurred and collagen formed later. In guinea pigs the lesions remained predominantly cellular, and these lesions were partly or wholly reversible.

"On intravenous injection in rabbits, cor pulmonale, hepatic cell atrophy, and interstitial nephrosclerosis were significant findings. All lesions except the renal damage proved to be reversible.

"The practical and theoretical significance of these observations is discussed."

[For Parts I to III, see this *Bulletin*, 1958, v. 33, 589, 590, 591.]

ENGLEBRECHT, F. M., YOGANATHAN, M., KING, E. J. & NAGELSCHMIDT, G. **Fibrosis and Collagen in Rats' Lungs produced by Etched and Unetched Free Silica Dusts.** *Arch. Indust. Health.* Chicago. 1958, Apr., v. 17, No. 4, 287–94, 8 figs. on 2 pls. [12 refs.]

"Intratracheal injection experiments on rats were made with vitreous silica, quartz and tridymite, before and after etching with NaOH, and with quartz and tridymite etched with HF before and after electrodialysis.

"The 10 samples, which all had similar size distributions with a mean diameter of about 1.5μ, were injected in amounts of 25 mg. per rat, and their effects were followed up to 220 days after injection by histological assessment of degree of fibrosis and chemical determination of collagen in the lungs, and by weighing the lymph glands.

"The samples showed a considerable range of fibrogenic activity: from 40 to 140 days were needed to reach Grade 5 fibrosis, and collagen production ranged from 19 to 150 mg. per 100 days, while controls without dust showed 5 mg. collagen per 100 days.

"The weight increases in the lymph glands varied for the different samples, but the variations were not as large as with the rates of collagen production.

"In conformity with previous work, vitreous silica was found to be less fibrogenic than quartz, and quartz less than tridymite. Etching by HF or NaOH increased

the activity of quartz, but had little effect on that of tridymite or vitreous silica. Electrodialysis reduced the activity of the samples etched with HF.

"As all unetched samples had high, and all etched samples (with one exception) low silica solubilities, there was no parallelism between fibrogenic activity and silica solubility. Alternative views on fibrogenic activity are briefly reviewed."

WATANABE, K. **The Influence of Radioactive Dust on Experimental Pneumoconiosis.** *Tohoku J. Exper. Med.* 1957, Aug. 25, v. 66, No. 2, 131–43, 14 figs.

"1. Experimental pneumoconiosis by inhalation of slight radioactive feldspar dust was developed in form of progressive fibrotic nodules in animal lungs.

"2. Experimental pneumoconiosis by inhalation of control non-radioactive feldspar dust was negative to make fibrotic nodules in the corresponding periods.

"3. Experimental pneumoconiosis by high radioactive allanite dust was rapidly and intensively developed in form of fibrotic nodules in animal lungs within short time.

"4. Experimental pneumoconiosis by control allanite with a slight radioactivity was not so severe, and the process of the fibrosis was slow and weak in comparison with the preceding case.

"5. From these results mentioned, we might conclude that the natural radioactivity of rocks, when its dusts are inhaled, will cause the formation of fibrotic nodules in the lungs."

VINCENT, D., EINBRODT, H. J., SPERLING, H., FITZEK, J. & BERNHARD, G. Silikose—ein Kombinationsschaden? Über die Radioaktivität von Fremdstäuben aus Lungen verstorbener Ruhrbergleute mit Silikose. **[Silicosis—a Damage due to Combination of Different Effects? On the Radio-activity of Dusts Isolated from the Lungs of Silicotic Coal-Miners from the Ruhr]** *Beiträge z. Silikose-Forschung.* 1958, No. 54, 15–29. [36 refs.]

This paper is mainly concerned with a critical review of the recent work of FLÜGGE (*Glückauf*, 1958, v 94, 185), who had stressed the fact that inhalation of radioactive dust leads to lung fibrosis and had suggested that pneumoconiosis of coal-miners, which is called silicosis in Germany, may be a combined effect of quartz and radiation damage. The radiation may come from the potassium isotope ^{40}K which is present in lung dusts mainly in the mica sericite, and thus the sericite theory of silicosis could be revived.

As ^{40}K is in fact likely to be the main source of radiation in lung dust, the (very low) activity of 3 such dusts isolated by the formamide method was determined and the estimated total potassium content was compared with chemical determinations of potassium. The values were found to be in good agreement.

However, the dust contributed only between one-tenth and one-third of the total potassium present in normal lung tissue, and a detailed discussion leads to the conclusion that the extra radiation due to dust is trivial compared with the radiation load carried normally both from ^{40}K and from cosmic radiation.

This is followed by a critical discussion of recent papers by WATANABE [this *Bulletin*, 1956, v. 31, 920; and above] and by BRUNNER and RÜTTNER [this *Bulletin*, 1957, v. 32, 871] on experimental silicosis. It is admitted that in animal experiments large X-ray doses together with quartz lead to stronger fibrosis than quartz alone, but it is considered to be extremely unlikely that the lung fibrosis of coal-miners could be due to a combined effect of quartz and radiation.

[The authors' detailed calculations, references and sound reasoning, make this a most useful paper.]

G. Nagelschmidt

SCHRÖDTER, S. & SAITMACHER, H. Über den röntgenologischen Nachweis der experimentellen Silikose beim Meerschweinchen. **[On the Radiographical Demonstration of Experimental Silicosis in Guinea Pigs]** *Arch. f. Hyg. u. Bakt.* 1958, Sept., v. 142, No. 6, 471–80, 3 figs. [13 refs.]

In the course of experiments, on guineapigs, concerned with the combined effects of intratracheally injected quartz and BCG inoculation, the need arose to follow the fibrosis of the lungs during life by X-ray radiography. The present paper gives a detailed account of the technique used and of some of the results obtained. It is illustrated by 4 radiographs.

The radiographs were obtained with a rotating anode tube, of 1·2 mm. focus, with exposures of 20–40 milliseconds at 44 KV and 13–22 MA from an AC installation with 6 rectifying tubes. Distance from the tube focus to the film was 40 cm. (16 inches), and no intensifying or secondary ray screens were used. The animals were fixed without anaesthetic, lying on a board on their backs with extremities extended and the head held by a ring.

Observations were made on guineapigs 6–7 months after intratracheal injection of quartz, and as the animals were killed shortly afterwards radiological and pathological observations could be compared. The results are given in a table and are discussed in detail. There was usually agreement between radiological and pathological observations, although discrepancies occurred. In further tests it could be demonstrated that X-ray shadows could be seen 6 weeks after injection of quartz dust.

In contrast to observations by VORWALD *et al.* [this *Bulletin*, 1954, v. 29, 961], BCG did not aggravate the fibrosis produced by quartz. *G. Nagelschmidt*

KRÜMMEL, H. Silikogene Gewebsreaktionen am Tierauge. **[The Reaction of the Eyes of Experimental Animals to Silica]** *Beiträge z. Silikose-Forschung.* 1958, No. 57, 1–127, 140 figs.

The English summary appended to the paper is as follows:—

"In long-term experiments with dust emulsions being injected into the anterior chamber and the vitreous body of rabbit eyes, the tissue reactions demonstrated bioptically and histologically were dependent on the kind of dusts employed. Working with regard to the problem of silicogenic tissue reaction quartz (crystalline SiO_2) and, for comparison, aerosil (amorphous SiO_2), and corundum (Al_2O_3 chemically inert) have been used

in a basic experiment. In this way it was possible first to compare the reactions on the silica persistent in crystalline form and on the amorphous soluble form and, in the second place the non characteristic foreign-body reaction to be expected from corundum could serve to define the possibly present analogous reaction towards the solid quartz particles versus the silica reaction.

"Pure quartz of small particle size is stored up by an epitheloid cell granuloma. Origin and development phases of this granuloma are still to be recognized at a late stage because its histological components are developing successively but simultaneously remain existing side by side and influence each other. Three principal phenomena are to be distinguishable morphologically:—

"1) The continuous emigration and propagation of quartz phagocytosing macrophages, in the majority modified pigmented epithelial cells.

"2) A progressive proliferation of the connective tissue (silicogenic fibrosis) with flowing transitions from a fine argentophile reticulum of reticulin fibres to a collagenous coarse-fascilular connective tissue and from this to an anuclear and quartz-free callosity. In the area of the retina a fibrogliosis results analogously to the quartz contact.

"3) Histolytic processes in form of local necrosis with tendency to calcification and degenerative ossification of the connective tissue.

"Contrary to the crystalline silica the amorphous silica (aerosil) proves as a tissue poison. The choroid membrane of the eye and retina become totally atrophic and necrotic respectively. No histocytic granuloma occurs. The fibroblastic reaction is considerably stronger; a steatosis of the primitive bone marrow occurs within the ossified callosities.

"Corundum forms secondary dust conglomerates causing atrophy from pressure in the surrounding tissue. The pigment epithelium remained without reaction. Fibrosis and glioses did not go beyond the initial stage. There was no necrosis.

"In further experiments it was tried whether it is possible to inhibit or change this per exclusionem defined tissue reaction through an addition of associated substances. Two working hypotheses formed the basis. It should be made out:

"1) Whether it is possible to neutralise the surface activity of the quartz crystal. For this milk of lime and sulphurated phenol were used.

"2) Whether it is possible chemically to throttle the reaction of free silica in the tissue by addition of calcium carbonate from which Ca-cations will be liberated. The results were as follows: The reaction of the macrophages was not influenced by any of the associated substances, the fibrosis only by milk of lime in a convincing way. The histolytic phenomena and the extreme osteoid sclerosis of the granuloma were inhibited by milk of lime and phenol, completely by the latter. In a control experiment with pure calcium carbonate an atrophy of the ciliary body occurred regularly, evidence that the substance is not harmless towards tissue. In mixed dust it dissociated from quartz. The fibrosis of the silicogenic granuloma suffered a morphological modification hereby.

"In a critical comparison of the histological findings the silicogenic tissue reaction on the crystalline form of silica proves as non identical with a mere foreign-body reaction. In deviation from this it shows the morphological picture of a progressive fractionated and protracted fibrosis with a tendency to terminal callosity and sclerosis."

LÜCHTRATH, H., FRIEBEL, H. & v. GRAEVENITZ, A. Chronische Peristonanwendung bei experimenteller Silikose. [**Prolonged Administration of Periston in Experimental Silicosis**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 4, 361–74, 3 figs. [Numerous refs.]

Polyvinylpyrrolidone in colloidal solution in physiological saline under the trade name of Periston (mean molecular weight of 30,000) has been used therapeutically for the replacement of blood fluids. Periston-N (mean molecular weight 12,600) has been employed in the treatment of oedema and also for other purposes such as a detoxicating agent and for the prevention of the formation of renal calculi. In some work on experimental silicosis it was shown that the development of typical silicotic nodules was much delayed if Periston-N was mixed with the colloidal silica before injection into the animal tissues.

In this paper there is a detailed account of experiments on rats (263 were used) which were designed to test the effect of Periston on the development of pulmonary silicosis. Intratracheal injctions of silica were administered to the rats by the method of KETTLE and KING. A group of these rats were given a parenteral injection of Periston or Periston-N on each of 3 days in each week throughout the experiment which lasted for 9 months. Another group of these rats was given daily inhalations of Periston in aerosol form. During the course of the investigation some of these 2 groups of rats were examined in respect of their cardiopulmonary function. About 9 months after the beginning of the work all surviving rats were killed. Specimens of lung, heart, kidney, liver and spleen from these and from animals which had died in the meantime were examined histologically and the degree of fibrosis was assessed. The findings are described fully with tables and photographs of tissue sections. There is a long discussion.

The results of the experiments were entirely negative in the sense that there was no demonstrable difference in the development of silicosis in the groups of rats treated with Periston or Periston-N and the control groups which had been given injections or inhalations of the Periston solvent alone. *M. E. Delafield*

TRASKO, Victoria M. **Silicosis, a continuing Problem.** *Pub. Health Rep.* Wash. 1958, Sept., v. 73, No. 9, 839–46, 2 figs. [17 refs.]

This article is based on a paper presented at the 9th annual meeting of the McIntyre Research Foundation, Toronto, Canada, on January 28, 1958. The author is non-medical and the essay is a historical review of the occurrence and incidence of silicosis in the U.S.A. The earliest recorded case (fatal) occurred

in a stove foundry worker in Poughkeepsie, N.Y., in 1887. In the same year a group of cases were observed at a cutlery factory. A report issued in 1900 recorded the deaths of 30 men, who contracted the disease after 1–2 years' exposure to dust from crushing quartzite ore in a gold assaying mill in Nevada. The examination in 1920 of 427 granite cutters in Barre, Vermont, revealed that practically all the workmen were suffering from silicosis or silicosis accompanied by tuberculosis. The most notable experience was the Gauley Bridge disaster in which, according to Congressional hearings held in 1936, 476 workers died from silicosis and 1,500 others were suffering from the disease which they contracted while digging a rock tunnel for diverting water to a hydro-electric plant during 1932–4. Since then an increasing number of States have introduced industrial hygiene programmes for the control of the disease.

Owing to the fact that the disease is not notifiable and that the diagnosis is frequently missed or not recorded on death certificates even in districts where the disease prevails, it is almost impossible to measure its prevalence. By assembling piecemeal information from official agencies, the author amassed information on 12,763 cases in 26 States, covering the period 1950–5. About 20% of patients were known to have died. In the entire United States over the same period 11,650 deaths—an average of about 2,000 per year—were recorded as due to occupational pneumoconioses. Tuberculosis, with mention of occupational disease of the lung, accounted for 28% of the 11,650 total; silicosis and anthracosilicosis for 60%; and unspecified and other pneumoconioses for 12%.

From the mortality statistics of Pennsylvania information was obtained on 1,519 deaths among silicotics for the 15-month period January, February and March 1953 (pilot survey) and the whole of 1954. Pneumoconiosis as a primary cause of death was assigned officially to 60% of this 1,519 total; other causes of death were assigned to 40%. Thus, 2 out of every 5 deaths among silicotics were attributed to other causes.

The following table summarizes the 1,519 death certificates and shows what other conditions were associated with silicosis:—

Frequency of other conditions mentioned on 1,519 death certificates listing silicosis, anthracosilicosis, or pneumoconiosis as a primary or contributory cause of death, January–March 1953, January–December 1954, Pennsylvania.

Condition	Number	Per cent
Only silicosis, anthracosilicosis, or pneumoconiosis mentioned ...	218	14·4
Respiratory tuberculosis ...	143	9·4
Cancer, respiratory system ...	50	3·3
Cancer, other sites ...	58	3·8
Cerebral haemorrhage, thrombosis ...	67	4·4
Heart and other disease of circulatory system ...	861	56·7
Bronchial asthma ...	67	4·4
Influenza, pneumonia, bronchitis ...	139	9·2
Ulcer, hernia, cirrhosis of liver and other disease of digestive system ...	60	3·9
Nephritis and other disease of genito-urinary system ...	57	3·8
Accidents ...	10	·7
Cor pulmonale ...	236	15·5
Emphysema ...	89	5·9
Pulmonary haemorrhage ...	35	2·3
Pulmonary oedema ...	61	4·0

Compensation for the disease is very expensive. There is need for more support for preventive activities by official agencies. Prevention is still cheaper than compensation. *A. Meiklejohn*

DOYLE, H. N., FLINN, R. H. & DREESSEN, W. C. **A Review of the Pneumoconiosis Problem in the United States.** *Amer. Indust. Hyg. Ass. J.* 1958, Aug., v. 19, No. 4, 317–23. [56 refs.]

Pneumoconiosis, and more particularly silicosis, has been the outstanding occupational disease disability problem of American industry for many years. This is illustrated by reference to the studies of TRASKO [see above]. The experience of the disease among granite cutters at Barre, Vermont, in 1920 is contrasted with that of a study made in 1956 which reveals the salutary effect of dust control measures introduced between 1935 and 1937. Whereas silicosis was diagnosed in 538 (40%) of the men employed before 1937, no case of the disease was identified among 1,134 men who started work in the granite industry in 1937 or later. This experience supports the adequacy of the standard of 5 mppcf (million particles per cubic foot) and indicates that, with proper engineering controls, the disease can be prevented.

The remainder of the article consists of a brief commentary on the pathogenesis of pneumoconiosis, lung disease in coal-miners and diatomaceous earth workers and developments in the environmental control of dust. *A. Meiklejohn*

APPELMAN, A. C. Enige bijzondere verschijningsvormen van antraco-silicotuberculose. [**Special Forms of Silico-Tuberculosis**] *Nederl. Tijdschr. v. Geneesk.* 1958, Mar. 22, v. 102, No. 12, 570–72, 2 figs. English summary (6 lines).

Histories are given of 4 cases of silicosis occurring in Dutch miners. (1) A man aged 62 who had worked underground for 17 years. There was a dense shadow at the right apex. At autopsy a silicotic pseudotumour was found. Nodulation was absent. (2) A man aged 36, who had worked underground for 17 years. Lobectomy was carried out, and a pigmented fibrous mass with caseous foci was found. Nodulation was absent. (3) A man aged 47 who had worked underground for 28 years, with heavy exposure to stone dust for 2 years. The right upper lobe was resected for tuberculosis; it was infiltrated with connective tissue with occasional nodule formation and extensive

caseation. Nodules were absent from the remaining lobes of the lungs. (4) A man aged 28 who had worked underground for 6 years. He developed tuberculosis at the left hilus, and nodulation was absent. At pneumonectomy the lung was indurated, with a tuberculous cavity surrounded by induration with pigmentation and a few silicotic nodules. In the cases described generalized nodulation was absent, and the author points out that the absence of this typical sign of silicosis may cause difficulty in obtaining compensation. *D. J. Bauer*

Uytdenhoef, A. Les risques de pneumoconiose dans les carrières de porphyre. [**Pneumoconiosis in Porphyry Quarries**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1958, June, v. 16, No. 6, 289–314.

In Belgium about 1,200 persons are at present employed in the quarrying of porphyry. The mineral is not true porphyry but a siliceous diorite of igneous origin. Formerly the material was used extensively in the construction of roads and pavements, but it has now been largely displaced by asphalt.

The quarrymen excavate the rock in large blocks, which are then trimmed to a convenient size. These are transported to the surface plant, where they are crushed and graded according to specification. To increase productivity the operations have been extensively mechanized during recent years. All the processes are dusty, particularly crushing and grinding.

The rock contains, on average, about 23% free silica. Most of the dust is of respirable size, 35–65% of the particles being under 3 microns in diameter and 63–84% under 5 microns. The dust cloud is of the order of several thousand particles per cc.

449 workmen, of whom 288 were still working and 161 pensioners, were submitted to radiographic examination of the lungs. The results were analysed by occupations, age-group and state of the lungs. Pulmonary fibrosis of silicotic type was diagnosed in 33 cases. These were classified as anteprimary 23 cases, stage I 6 cases, stage II 2 cases, and stage III 2 cases. In 2 patients the silicosis was accompanied by tuberculosis. [This is a routine local field survey, which raises no new matter of general interest. It does underline the fact that mechanization of quarry and mining operations can greatly increase dust risks.]

A. Meiklejohn

Schmid, H. J. Bemerkungen zur Giesserei-Silikose. [**Observations on Silicosis in Foundries**] *Ztschr. f. Unfallmed. u. Berufskrankh.* 1958, Sept., v. 51, No. 3, 221–31, 4 figs. [12 refs.]

This is a paper presented at the 43rd Annual Meeting of the Swiss Society of Industrial Disease and Accident in November 1957. It is based on the experience of the author in Schaffhausen where, as a result of technical hygienic measures, silicosis in sand blasters has for practical purposes disappeared. In contrast to this the introduction into industry of screening and other routine X-ray examination has brought to light a surprising number of cases of pneumoconiosis in foundry workers engaged in a variety of jobs other than that of sand blasting. With improvement in the methods of examination the diagnosis of silicosis in foundry workers has increased steadily. In 1944–49 the incidence found by the author was 11% and in 1955 the incidence reported by another observer was 30%. In a special examination of 20 workers exposed to the dust of emery, which contains but little silica, the incidence of silicosis in these men who had worked at their job for over 10 years was over 50%. Silicosis in foundry workers, in contrast to that of sand blasters in the past, is in general considered to be a mild condition which may not give rise to any symptoms or disability. This view is held by many observers and is here discussed at length with reference to published reports and the experience of the author, who is of opinion that the form of silicosis found in these workers is not to be regarded as a negligible condition. There is also a discussion on bronchitis and conditions of asthmatic type in foundry workers which may be caused by silicosis but may, on the other hand, be due to non-specific irritation by dust or be of allergic nature.

M. E. Delafield

Higgins, I. T. T. & Cochran, J. B. **Respiratory Symptoms, Bronchitis and Disability in a Random Sample of an Agricultural Community in Dumfriesshire.** *Tubercle.* 1958, Oct., v. 39, No. 5, 296–301.

In 1957 Higgins [this *Bulletin*, 1958, v. 33, 238] recorded the results of an investigation into the prevalence of respiratory symptoms, bronchitis and disability in a random sample of an agricultural community living in the Vale of Glamorgan in South Wales. The results for the men aged 55–64 who had not worked in either mining or quarrying were compared with previous findings for non-miners in the industrial town of Leigh in Lancashire. While a higher prevalence, which was not, however, statistically significant, of an arbitrarily defined level of "chronic bronchitis" was observed in Leigh, there was in general a remarkable similarity in the prevalence of the individual respiratory symptoms in the 2 areas. This was surprising in view of the probable differences in the amount of atmospheric pollution between them and raised the question as to how representative of rural areas is the Vale of Glamorgan. [Professor R. E. Lane, Manchester, at a meeting in London submitted that Leigh did not represent a heavily smoke-polluted Lancashire town.] In an attempt to answer this question a parallel investigation of a random sample of men and women aged 55–64 living in Annandale, Dumfriesshire, Scotland, was carried out.

The cooperation of the local inhabitants was excellent so that approximately 90% of the random sample were included in the analysis. The prevalence of respiratory symptoms was broadly similar to that observed in the comparable age-group (55–64) in the Vale of Glamorgan. The authors conclude that the results suggest that the 2 areas do not differ significantly in the amount of bronchial disease present, and further that while an industrial environment, including atmospheric pollution,

is responsible for a small amount of chronic bronchitis and disability, the effect is less than is usually supposed.
A. Meiklejohn

WORTH, G., IBEL, E., DURBEN, H. H. & GASTHAUS, L. Über die Häufigkeit von Silikose, Bronchitis und Emphysem bei Steinkohlenbergarbeitern am linken Niederrhein. [**Incidence of Silicosis, Bronchitis and Emphysema in Coal-Miners in the Lower Rhine Area**] *Beiträge z. Silikose-Forschung.* 1958, No. 56, 1–26, 2 figs.

The English summary appended to the paper is as follows:—

"The frequency of bronchitis, emphysema and silicosis of 9935 coal-miners—total personnel employed underground by 4 large mines on the left Niederrhein—is ascertained in relation to age and time of exposition. 2125 coal-miners (= 21.4%) had pneumoconiotic lesions of the lungs. In 678 (= 6.82%) cases the authors found a bronchitic syndrome, and 393 coal-miners (= 3.95%) showed signs of an emphysema of the lungs. The frequency of bronchitis as well as of emphysema remarkably increased with age and with duration of underground work respectively.

"Besides the investigation of all cases of bronchitis and emphysema of coal-miners still in full employment we ascertained furthermore about 2815 coal-miners of the same region who in the years 1948—1954 changed their working place or left the mine on account of any disease. In 181 cases (= 6.43%) this was caused by bronchitis, and in 110 cases (= 3.91%) by emphysema.

"These figures give, according to our opinion, a representative idea of the frequency of bronchitis and emphysema in coal-miners on the left Niederrhein. They might be of essential value to enlighten the question of a causal connection between bronchitis, emphysema, and occupational influences, if corresponding results of an examination of other occupations without dust hazard are available in the same geographical area."

HOFFMANN, H. & WORTH, G. Über die Häufigkeit von Nasennebenhöhlenveränderungen bei Kohlenbergarbeitern am linken Niederrhein. [**Incidence of Nasal Sinus Changes in Coal-Miners in the Left Lower Rhine Area**] *Beiträge z. Silikose-Forschung.* 1958, No. 56, 27–39.

The English summary appended to the paper is as follows:—

"185 = 18.5% of 1000 coal-miners having worked underground for 8 years at least showed pathological radiographs of the nasal sinuses. There were no significant accumulations at a certain stage of silicosis. Confronting miners with normal and pathological stages of the nasal sinuses in dependence of simultaneous bronchitis those with pathological findings of nasal sinuses generally showed a higher frequency of bronchitis regardless whether they had silicosis or not."

KING, E. J., YOGANATHAN, M., HARRISON, C. V. & MITCHISON, D. A. **Experimental Infective Pneumoconiosis. V. Massive Fibrosis of the Lungs produced by Coal-Mine Dust and *Mycobacterium tuberculosis* var. *muris* (Vole Bacillus).** *Arch. Indust. Health.* Chicago. 1957, Nov., v. 16, No. 5, 380–92, 8 figs. on 2 pls. [36 refs.]

"The combined actions of live vole bacilli with coal or coal-mine dusts (containing 20% of siliceous matter, shale) and of BCG plus coal-mine dust and the individual effects of live vole bacilli alone have been studied by the intratracheal injection of these substances into the lungs of guinea pigs.

"Vole bacilli alone produced a regressive type of tuberculosis. The peak of the disease was reached at about 90 days, and by 365 days there was complete resolution of the lesions in many of the animals. A few, however, showed small calcified nodules and scar tissue, while in all of them there was evidence of lymphoid hyperplasia even at the end of one year.

"The combined actions of vole bacilli and the various dusts resulted in proliferative, necrotic, and extensive tuberculous lesions involving large areas of lung tissue.

"The disease reached a peak at 120 to 150 days. At the end of one year there was only partial resolution.

"Coal-mine dust combined with BCG produced lesions which were less severe than those due to vole bacilli plus dusts. The lesions increased in severity up to about 100 days and then gradually regressed over a period of one year. There was no necrosis or calcium deposition in any of the lesions.

"Vole bacilli were injected (in another experiment, Yoganathan), together with and at varying intervals after the coal dust, into the lungs of rats. After 30 days there was no significant difference found in the various groups, suggesting that the time factor did not alter the result in any way. The lesions increased in severity up to about 150 days and then gradually became less cellular, more contracted, and fibrotic.

"The similarities between the progressive massive fibrosis of coal-miners' pneumoconiosis and the experimental results are discussed."

MÜLLER, G. & HÜBNER, O. Untersuchungen an einer Talk-Staublunge. [**Investigations of Pneumoconiosis caused by Talc**]. *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 3, 352–4, 2 figs.

In this short paper there is an account of the examination of the lungs of a deceased worker in talc by means of X-ray pictures of the mineral matter extracted from them. The procedure adopted was to treat a piece of lung about the size of a match box with a mixture of nitric acid and perhydrol for some weeks at a temperature of 80°C. in order to remove organic matter. The residue of concentrated mineral matter was then examined by X-ray diffraction. A photograph of the spectrum so obtained is given, together with the spectra obtained with pure talc dust and with untreated talc lung. This comparison shows the value of prior removal of organic matter in that

the X-ray diagram is more definite and also shows lines which are not visible in the untreated lung.

M. E. Delafield

GÄRTNER, H. & HERZOG, W. Überlegungen zur Pathogenese eines Falles von Pneumokoniose aus dem Erzbergbau. [**Considerations of the Pathogenesis of a Case of Pneumoconiosis in a Worker in an Iron Mine**] *Arch. f. Hyg. u. Bakt.* 1958, Feb., v. 142, No. 1, 65–80, 4 figs. [17 refs.]

In this there is a long, detailed medical and pathological description of a case of pneumoconiosis in a man who had worked for about 30 years as a miner in an iron mine. The dust of the mine contained little silica, but in the course of his employment he had been diagnosed as a case of silicosis. The findings at autopsy, the results of chemical analysis of the lungs and the changes in the lungs of rats that had been given intracheal injections of sinter dust (which contains 58% of iron oxides and less than 1·0% of free silica) are detailed and discussed at length. Chemical analysis of the lungs showed predominantly iron and phosphorus but no silica. Nevertheless, it is assumed that silica was deposited in the lungs at times in the course of the years and so led to silicotic changes. The silica was absorbed later and fibrogenic changes then ceased; this view is in accord with the clinical course in this case and the chemical findings.

M. E. Delafield

RUZDIC, I. & ČREPINKO, I. Das Blei als Hemmstoff der Katalasewirkung. [**Inhibition of Catalase by Lead**] *Hoppe-Seyler's Ztschr. Physiol. Chem.* 1958, v. 312. Nos. 1/3, 22–5, 3 figs. [14 refs.]

In this paper some account is given of published work on the effect of various chemicals, including heavy metals, in inhibiting or accelerating enzymic action. The experimental work which is here described was undertaken to study the influence of lead on catalase because of its possible importance in causing the anaemia which occurs in lead intoxication. A short report with charts shows that the lead ion (lead nitrate) definitely inhibits the catalase action of blood serum. It was, however, noted that this inhibition occurs only when the serum is treated with the lead salt for 30 minutes before being incubated with the substrate.

M. E. Delafield

DINMAN, B. D., EVANS, E. E. & LINCH, A. L. **Organic Mercury. Environmental Exposure, Excretion, and Prevention of Intoxication in its Manufacture.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, No. 3, 248–60, 10 figs. [27 refs.]

Over 5 years of experience in the manufacture of organic mercury salts at Chambers Works has confirmed that a safe threshold limit for organic mercury is 0·1 mgm. per cubic metre of air. Others have suggested this is 10 times too high (2,3,4) but the authors suggest that the analytical details of some of the European studies may not have been accurate.

20 men exposed to mercury in air over 0·01 mgm. but less than 0·1 mgm. per cubic metre were studied. The exposure was derived from the dust of ethyl mercury chloride adsorbed on inert clay and from solvent solutions of ethyl or phenyl mercury acetate.

Clinical findings were based on monthly physical examinations, urine analyses and on more elaborate annual examinations. All men with a mercury level of more than 0·1 mgm. per litre of urine were removed from exposure until they were below a figure of 0·05 mgm. per litre for a fortnight.

Detailed estimations of exposures were made and methods used are fully described and results are recorded. A table of subjective symptoms and their incidence is also recorded. Significant complaints of exposed workers did not appear to occur with greater frequency than in a control group. The signs and symptoms reported by Scandinavian workers at urinary mercury levels of 0·05 to 0·1 mgm. per litre could not be confirmed.

The studies confirmed that mercury excretion fluctuates irregularly. After cessation of exposure excretion continues for a long time and rises to a peak before decreasing in an irregular manner.

An effective health control programme is described, and the limited value of atmospheric threshold limits for this purpose is discussed. *T. O. Garland*

MATTHES, F. T., KIRSCHNER, R., YOW, Martha D. & BRENNAN, J. C. **Acute Poisoning associated with Inhalation of Mercury Vapour. Report of Four Cases.** *Pediatrics.* Springfield, Ill. 1958, Oct., v. 22, No. 4, Pt. 1, 675–88, 9 figs. & 1 coloured pl. [16 refs.]

This is a report on a recent experience of 4 patients with a severe atypical form of pneumonitis associated with the inhalation of mercury vapour. On an afternoon in February 1957 a Negro mother aged 19 years who had 3 children, aged 30 months, 20 months and 4 months, painted a small gas space-heater with a paint consisting of about 40–60 ml. of aluminium paint, 80–100 ml. of turpentine and 300–350 ml. of mercury. As the paint would not stick she lit the gas and allowed it to burn all night. The family were well when they went to bed in their small 2-room house but during the night the mother felt ill with abdominal cramps, diarrhoea, shortness of breath and cough and the children were restless and had some respiratory difficulty. In the morning the family went to a clinic where they were treated for upper respiratory infection since the history of the mercury paint application was not known at that time. Afterwards they went to the grandmother's home where their condition got worse. A physician was consulted by telephone because of the serious state of 1 of the children and symptomatic care was continued. During that night all the patients got worse and at 8 a.m. one of the children a little girl aged 20 months, died. In the morning the mother and the 2 living children were admitted to hospital where the 30-month-old child died 30 hours after admission and the 4-month-old infant also died after 4 days.

There is a full account of the clinical course of the poisonings and of the results of investigations with tables, figures, X-ray photographs of the lungs and

plain and coloured photographs of tissue sections. There is a discussion of these findings with reference to the relevant literature. The poisonings were characterized by the sudden onset of rapid respiration, cough, fever, gastro-intestinal disturbances and central nervous system manifestations. The outstanding pathological post-mortem findings were erosive bronchitis, bronchiolotis and severe interstitial pneumonitis. Quantitative analyses of the urine for mercury were suggestive but not diagnostic. Substantially increased mercury content was found in the lungs, liver and spleen in 2 of the cases. The treatment of mercury poisoning by the early administration of BAL [dimercaprol] and of supportive measures is also considered.

M. E. Delafield

WOODCOCK, S. M. **A Case illustrating the Effect of Calcium Disodium Versenate ($CaNa_2E.D.T.A.$) on Chronic Mercury Poisoning.** *Brit. J. Indust. Med.* 1958, July, v. 15, No. 3, 207–8, 1 fig.

"A case of chronic mercury poisoning treated with 2:3 dimercaptopropanol (B.A.L.) and intravenous calcium disodium versenate ($CaNa_2E.D.T.A.$) is reported.

"Contrary to previous reports, $CaNa_2E.D.T.A.$ resulted in increased urinary excretion of mercury, while B.A.L. did not.

"It is concluded that $CaNa_2E.D.T.A.$ is of value in the treatment of chronic mercury poisoning."

BISTER, F., KLAVIS, G., KÖHLER, H. & WITTGENS, H. Zur Gewerbetoxiologie von Anstrichstoffen auf Zinkchromatbasis. **[Industrial Poisonings due to Zinc Chromate Paints]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 567–87, 10 figs. [22 refs.]

Zinc chromate paints have come to be used to a considerable extent in Germany as anti-corrosion paints and are often applied by a spray method. To study the possible toxicity of the paint experiments on rabbits were carried out. The animals were submitted to the intratracheal instillation of the separate constituents of the paint—the pigment, the binding constituent which contains phthalate, the solvent constituent—and the paint ready for use. To some other animals these constituents of the paint were administered by stomach tube. The urinary excretion of chromium during the next 2 days was determined and then the animals were killed and histological examination of the lungs were carried out. A full clinical examination of 14 paint sprayers was also made with X-ray examination of lungs, blood examination and determination of urinary chromium excretion. The findings of the study are described at length with tables and photographs of the histological appearances of the animal lungs.

It was found that the chromate pigment dust produced marked changes in the mucous membranes of the respiratory tract and furthermore that the finished paint has even greater effects. There is evidence that this increased effect is due to the binders containing phthalate, which are in the paint, for these when administered alone also had a great irritant action. In comparison with the animal results, the clinical examination of the painters yielded no significant evidence of toxic damage. Nevertheless it is considered that the precautions of effective masks and good ventilation should not be relaxed, and that workers with zinc chromate paint should have routine clinical examinations with special attention to nose and throat and also urinary examination for chromate excretion. Yearly X-ray examination of the lungs is also recommended.

M. E. Delafield

SCHRENK, H. H. & SCHREIBEIS, L., Jr. **Urinary Arsenic Levels as an Index of Industrial Exposure.** *Amer. Indust. Hyg. Ass. J.* 1958, June, v. 19, No. 3, 225–8, 1 fig.

Urine analyses are commonly used for evaluating exposures to metallic elements. The results provide a measure of absorption and thus give an index of the magnitude of exposure, but are not necessarily proof of poisoning. In the course of urine analyses in a pilot plant operation in which there was a possibility that arsine could be generated, occasional values exceeding 0·5 mgm. of arsenic per litre of urine were found. Investigation ruled out exposure in the pilot plant as a significant source of arsenic, and medication was also excluded. The question of arsenic in foodstuffs was then raised. MONIER-WILLIAMS (*Trace Elements in Food.* 1949. New York: John Wiley & Sons, Inc.) has pointed out the high level of arsenic in sea food, and attention was then directed to this item in the diet of personnel in the plant.

During the course of this study approximately 1,000 determinations were made of arsenic in the urine of persons in the pilot plant and other plant areas. The results of these tests are given in detail in a number of tables. They indicate that, in the absence of unusual amounts of arsenic in the diet or other exposure to arsenic, the urine level in the majority of cases may be expected to be less than 0·1 mgm. per litre. The average values for groups after eating sea food ranged from 0·13 to 1·35 mgm. per litre. Additional experiments in 3 subjects demonstrated that the high levels of arsenic in the urine following a sea food meal were not maintained for more than 48 hours. The results obtained also demonstrated that high urinary arsenic levels may occur with no evidence of any adverse clinical effects.

The authors conclude that urinary arsenic values do not provide a reliable index to industrial exposure although, in a group of exposed persons, they may serve to check the efficacy of control measures and indicate if excessive absorption of arsenic occurs.

[Fortunately, or unfortunately, the customary diet of the average workman or factory hand in Britain does not include the sea foods rich in arsenic, *viz.*: oysters, lobsters, prawns, mussels, scallops and clam chowder. Nevertheless, this is a thought-provoking paper.]

P. J. R. Challen

DOLL, R. **Cancer of the Lung and Nose in Nickel Workers.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 217–23.

This is a statistical analysis of the death certificates held in the public health departments of districts where

workers in a nickel refinery lived. They include all males over 15 who died there in the period 1948–56 and those male residents who died elsewhere—15,247 in all.

Among the nickel workers the number of deaths observed from lung cancer was nearly 5 times the number expected. In a study of proportional mortality of this kind a number of alternative explanations for such a finding are possible. These are discussed. The risks of lung cancer among those employed directly on the process appears to have been approximately double that among the other employees in the refinery.

29 nickel workers died of nasal cancer in the period 1938–1956, some 200 or 300 times the number expected based on national figures.

The total number of deaths from these 2 types of nickel cancer known to have occurred in Britain is 188 (lung cancer 126, cancer of nose 62). Doll produces statistical evidence that the risk has been largely or completely removed in the last 35 years.

T. O. Garland

MORGAN, J. Gwynne. **Some Observations on the Incidence of Respiratory Cancer in Nickel Workers.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 224–34, 4 figs.

This paper is based on experience at the Mond Nickel Company's refinery at Clydach in South Wales. The carbonyl process for extracting nickel is described together with modifications that have taken place in the plant since 1933.

Bradford HILL was asked in 1939 to report on the statistical significance of certain cases of lung cancer that had occurred among the workers. He found a striking excess over the expected number of deaths from lung cancer and from nasal cancer. These deaths were confined to the process workers. The minimum duration of exposure was 15 months for cancer of the lung and 6 years for cancer of the nose. The "lag" period of either cancer may be 25 years or more. No nasal cancers have been recorded in persons who entered the works after 1924 but 6 lung cancers have been recorded as against 4 expected on the bases of national rates.

Various tables are included showing cancer rates in different groups of nickel workers and for different years of entry to the works and relating death to years of exposure.

It is considered that the carcinogen was possibly carried in the arsenic of the heated calcined dust. Before 1924 this dust probably contained arsenic from the sulphuric acid used.

Measures now taken to exclude metallic arsenides from the process, to provide arsenic-free sulphuric acid, and to suppress dust are briefly described.

T. O. Garland

WILLIAMS, W. J. **The Pathology of the Lungs in Five Nickel Workers.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 235–42, 12 figs. [19 refs.]

Of the 5 men concerned in this investigation, all of whom worked at nickel refining, 1 is alive and well 18 months after pneumonectomy for squamous carcinoma, 1 died 9 months after a similar operation for the same reason (only the lung removed at operation was available for study), at necropsy the other 3 were found to have died, respectively, of squamous carcinoma, alveolar-cell carcinoma and cor pulmonale. In this last case there was no tumour but cystic changes were evident in the lungs, together with bronchiectasis and generalized diffuse fibrosis.

The pathological findings of all these cases together with occupational exposure to nickel are summarized in tables, and there are 12 excellent photomicrographs illustrating histological findings.

The cases bear out the opinion that the squamous variety of lung cancer predominates where an industrial cause is responsible. The epithelium of non-respiratory and respiratory air passages was examined for any changes that might indicate a pre-malignant state. There was evidence of chronic inflammation but no definite pre-malignant epithelial changes.

2 patients showed honeycomb or "cystic change"—this is not diagnostic of industrial lung disease. Pulmonary fibrosis was present in all 5 cases, involving predominantly the interstitial tissue and without specific localization. There was no resemblance to silicosis.

Nickel and copper were present in excess in the 2 cases analysed, but no arsenic could be detected. [It is of interest in view of DOLL'S paper (see above) that of the 4 men with cancer, 1 started work in 1922 and 2 of the other 3 after 1924 when the re-organization of the processing plant took place.]

T. O. Garland

WEST, B. & SUNDERMAN, F. W. **Nickel Poisoning, VII. The Therapeutic Effectiveness of Alkyl Dithiocarbamates in Experimental Animals exposed to Nickel Carbonyl.** *Amer. J. Med. Sci.* 1958, July, v. 236, No. 1, 15–25, 1 fig. [17 refs.]

The dithiocarbamates are strong complexing agents which are used as reagents for the detection of cadmium, cobalt, copper, lead, manganese, mercury, strontium and nickel. They have also been shown to possess chemotherapeutic properties. This paper is concerned primarily with the antidotal properties of the dithiocarbamates in experimental animals (C-57 strain mice and Wistar strain rats) exposed to lethal inhalations of vaporized nickel carbonyl. Studies on Antabuse and Penicillamine [dimethylcysteine] are also reported. It has been shown that Antabuse (tetraethylthiuram disulphide) is reduced to diethyldithiocarbamate *in vivo*.

Of the various derivatives investigated the sodium salts of diethyl, dimethyl, diisopropyl dithiocarbamic acids and sodium morpholine dithiocarboxylate appear to be the most effective. Of these 4, sodium diethyldithiocarbamate (Dithiocarb) is the least toxic. Dithiocarb administered intraperitoneally in dosages of 50 or 100 mgm. per kgm. of body weight provided complete protection against the otherwise lethal effects of nickel carbonyl in concentrations from 0·048 to 0·30 mgm. per litre of air in mice, and 0·50 to 1·99 mgm. per

litre in rats. Dithiocarb administered orally also provided moderate protection in a dosage of 100 mgm. per kgm. of body weight. Greater amounts of nickel were excreted in the urine and faeces of rats exposed to the vapours of nickel carbonyl and treated with Dithiocarb than in surviving untreated animals similarly exposed.

The mechanism by which Dithiocarb counteracts the acute toxic effects of exposure to nickel carbonyl is speculative. It is a reasonable assumption that Dithiocarb as a chelating agent combines with the nickel in the tissues of animals poisoned with nickel carbonyl to form a non-toxic chelate. It is noteworthy, however, that other chelating agents such as calcium disodium ethylene diamine tetra-acetic acid are ineffective. Clinical studies in human beings accidentally exposed to nickel carbonyl who have received Dithiocarb therapeutically are reported in an accompanying paper.

P. J. R. Challen

SUNDERMAN, F. W. & SUNDERMAN, F. W., Jr. **Nickel Poisoning, VIII. Dithiocarb: a New Therapeutic Agent for Persons exposed to Nickel Carbonyl.** *Amer. J. Med. Sci.* 1958, July, v. 236, No. 1, 26–31, 1 fig.

Nickel carbonyl is one of the most toxic chemicals encountered industrially. Hazards from exposure may arise from a variety of operations. These include: (i) the separation of nickel from its ores; (ii) the preparation of intermediates in organic syntheses, sometimes under extremely high pressures; (iii) electroplating operations as a medium for depositing thin layers of metallic nickel in electronic circuits and magnetic tapes; and (iv) inadvertent formation whenever carbon monoxide comes into contact with an active form of nickel. Severe symptoms may develop insidiously hours or even days after exposure. This paper is concerned with clinical observations on 11 persons accidentally exposed to nickel carbonyl and treated with sodium diethyldithiocarbamate (Dithiocarb). It is noteworthy that aqueous solutions of Dithiocarb are alkaline. Epigastric discomfort following ingestion may be minimized by the simultaneous administration of a buffer, such as sodium bicarbonate. For parenteral administration the chemical is buffered with monosodium phosphate to yield a solution of *p*H 7·4. In the exposed persons the manifestations of poisoning were relieved after the ingestion of Dithiocarb. Delayed reactions were minimal and convalescence was uneventful. On the day after the administration of Dithiocarb the concentration of nickel in urine became increased in each of the 6 patients subjected to severe exposure. With continued therapy the concentrations of nickel in urine gradually decreased and reached approximately normal levels within 16 days after exposure.

[This is a valuable contribution and readers are strongly recommended to read the original. The medical management of intoxicated cases is described in some detail.]

[For references to earlier parts, see this *Bulletin*, 1958, v. 33, 593.] *P. J. R. Challen*

WOOD, C. H., BALL, K. P. & TEARE, N. D. **A Case of Beryllium Disease.** *Brit. J. Indust. Med.* 1958, July, v. 15, No. 3, 209–12, 4 figs. [12 refs.]

"The occupational and clinical histories and post-mortem appearances of a man who developed dyspnoea and cough while working with beryllium oxide are reported. The disease progressed, and, despite a temporary remission under treatment with corticotrophin, he died at 40 years of age after having been bedridden with dyspnoea for four years.

"Some of the difficulties of confirming the diagnosis of beryllium disease are discussed."

STRENGE, K. Eine Methode zum Nachweis geringer Selenmengen in der Luft und in biologischem Material. [**A Method for the Determination of Small Amounts of Selenium in the Air and in Biological Material**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 588–91, 2 figs.

Selenium is being used increasingly in many industries, for example in the manufacture of coloured glass, paints and inks, in alloys, in the rubber industry and in making photo-electric apparatus. It is also an impurity of certain minerals used in other industries. The present methods of analysis are inadequate since minute amounts of selenium and its compounds are extremely poisonous; in the United States the maximum allowable concentration recommended is 0·1 μgm. per litre in air.

The method described in this paper is a modification of the adaptation by CHENG (*Analyt. Chem.*, 1956, v. 28, 1738) of the procedure suggested by VON HOSTE. There is a detailed, technical account of the method as used for the analysis of selenium in air, in blood and other tissues and in urine. The procedure is based on interaction between selenic acid and diaminobenzidine followed by photometric measurement.

The accuracy of the method is stated as ± 10% with amounts of 5–20 μgm. Se and as ± 20% with 1–5 μgm. Se. *M. E. Delafield*

ZTSCHR. F. PRÄVENTIVMED. Zürich. 1958, Aug.–Sept., v. 3, Nos. 8/9, 283–92. Symposium sur les risques d'intoxication par les solvants industriels. [**Hazards of Poisoning by Industrial Solvents**]

This symposium of papers on the toxic hazards of solvents used in industry was organized by the Swiss Society of Preventive Medicine in conjunction with industrial hygiene and medicine groups in different parts of the country.

(1) *Les solvants industriels*—general introduction by C. GUERJIKOFF (Geneva): this paper is to be published at a later date.

(2) *Risks of Benzene in the Printing Trade* by M. LOB (Lausanne). This is a short communication in which there is mention of a paper published in 1956 on investigations made in a printing works and an account of a new enquiry at a small printing workshop in which 4 persons are employed. These workers are exposed at various stages of the printing processes to the fumes of crude solvents, some of which contain benzene, which are present in the inks and are used

for other purposes. Neither the owner of the works nor his employees had any symptoms or signs of illness but his wife and daughter, both of whom worked at the printing, had a slight anaemia.

(3) *The Toxicology of Trimethylbenzene* by E. GRANDJEAN, L. ROSSI and K. BÄTTIG. This paper was published in full in 1956 (*Rev. Méd. préventive*, 1956, v. 1, 389).

(4) *Investigations of the Effects of Carbon Disulphide in the Viscose Industry* by R. MÜNCHINGER (Zürich). This is a preliminary account of the results of a study of 100 workers, aged from 24 to 66 years, who had been exposed for periods ranging from 1 to 39 years to the fumes of carbon disulphide at a Swiss artificial silk factory. Analyses of the factory air at certain points showed the average concentration of carbon disulphide ranged from 5 to 35 mgm. per cubic metre which is well below the maximum allowable concentration of 60 mgm. per cubic metre. General medical and psychiatric examinations were carried out. About two-thirds of the workers complained of disturbed sleep, marked tiredness at work, irritability and intolerance of alcohol. In about one-third of the employees there were symptoms of digestive disturbance and signs of pathological changes in the cardiac, circulatory and respiratory systems. Disturbances in the vegetative, peripheral and central nervous systems were found to exist in two-thirds of the workers.

(5) *Carbon Tetrachloride and Digestive Troubles* by C. GUERJIKOFF. This paper is to be published later.

(6) *Non-specific Symptoms and Syndromes in Poisonings by Solvents* by F. BORBÉLY (Zürich). In this paper the author gives it as his opinion, based on a long experience, that the symptoms of poisoning by various toxic industrial solvents are non-specific in the sense that they cannot be used to differentiate between the possible causes of the poisoning because they are so similar in all solvent poisonings. This view is discussed. In a reconsideration of the subject a careful analysis was made of the symptoms and signs in 6 cases of trichlorethylene and 9 cases of carbon disulphide poisoning in which the patients had been exposed only to these 2 solvents. A table sets out the comparative findings in these cases in detail; the stages of poisoning are considered to be: (1) the prenarcotic and narcotic stage, (2) the transition stage in which there is evidence of encephalitis, and (3) the stage of organic damage to the nervous, hepatic and respiratory systems. In this analysis only minor differences between the symptomatic effects of the 2 solvents were found and these results accord with the notion of non-specificity.

(7) *Investigations on Trichlorethylene in Mechanical Industry* by E. GRANDJEAN, R. MÜNCHINGER, P. A. HAAS and H. K. KNOEPFEL. This was published in full in 1956 (*Rev. Méd. préventive*, 1956, v. 1, 13).

(8) *Poisonings by Perchlorethylene* by M. LOB (Lausanne). Perchlorethylene has frequently replaced trichlorethylene as a solvent for cleaning metals in industry since it was reported to be less poisonous because of its lesser volatility. Nevertheless it may cause serious toxic effects as is shown by the full reports which are given here of 2 men who were seriously poisoned by the solvent with ultimate chronic changes in the central and peripheral nervous systems. It would appear that the 2 workers had both worked under conditions of imperfect ventilation. It is concluded that the same strict measures of prevention should be used for perchlorethylene as for trichlorethylene.

M. E. Delafield

BÄTTIG, K. GRANDJEAN, E., ROSSI, L. & RICKENBACHER, J. Toxikologische Untersuchungen über Trimethylbenzol. **[Investigation of the Toxicity of Trimethylbenzol]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 555–66, 5 figs. [14 refs.]

Because of its toxicity benzol has been replaced by substances such as xylol, toluol and others for industrial purposes. These substitutes have all been studied extensively and found to have toxic effects similar to those of benzol. A more recent substitute—trimethylbenzol—has now been introduced and is the subject of the work reported in this paper. The product which was examined was a paint diluent of trade name Fleet-X DV99. On analysis it was found to consist of a number of different trimethyl benzols, particularly 1, 2, 4-trimethylbenzol (50%) and 1, 3, 5-trimethylbenzol (30%). The industrial medical part of the study was carried out at the painting department of a transport undertaking where the conditions of work of the men and the concentration of the solvent in the atmosphere were investigated. In addition 27 men exposed to trimethyl benzol and 10 men not so exposed were given a general clinical and a short psychiatric examination. A differential blood count was also made with determination of vitamin C deficiency. The animal experiment part of the study was carried out on rats. LD50 was determined by intraperitoneal injection and found to be 2·6 cc. per kgm. Rats were exposed to various concentrations of the solvent in the air for various periods of time. The results are described and set out in tables and charts in terms of mortality, general state of the animal, weight, water uptake, food uptake, renal function, urinary phenol excretion and the blood picture. In addition histological examination of liver, kidneys, spleen, pancreas, heart, lungs and adrenals was carried out.

The results of investigation of the men exposed to trimethylbenzol (found to be present in the air of their work places in an amount of 10–60 p.p.m.) were that a considerable number had hyperchromic anaemia, chronic bronchitis of asthmatic type, abnormal blood coagulation and gave evidence of depression of the central nervous system. In the rats it was found that the exposure to inhalation of air containing 500–1,700 p.p.m. of the solvent inhibited growth. Long exposures caused blood changes, diuresis, marked effect on the central nervous system, increased urinary phenol excretion, fatty changes in the liver and hyperaemia of the lungs with thickening of the alveolar walls.

M. E. Delafield

EHRLICHER, H. Benzidin in arbeitsmedizinischer Sicht. **[Benzidine: Industrial Medical Aspect]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1958, Sept., v. 8, No. 9, 201–7, 4 figs. [21 refs.]

A short historical account of the development of synthetic dye stuffs for textiles precedes some account

of the use of benzidine and its derivatives in the manufacture of azo-dyes. There is also an account of the gradual realization that in workers in these chemical processes there was an incidence of bladder tumours greater than that observed in the general population. Some points on the toxicology of benzidine, its entry into the body of the worker mainly through the skin but also by inhalation and ingestion, and its mode of action are considered briefly.

An investigation was carried out on workers exposed to benzidine. The description of this includes chemical particulars of the stages of the synthetic process and the amounts of aromatic amines found in the urine of men working at different jobs in this manufacture in the year 1939 and the individual years from 1951 to 1958. The analytical techniques for the examination of the urine of benzidine workers are described at some length. The technical measures that are to be adopted in benzidine factories to lessen the exposure of workers to the substance and also the hygienic measures of prophylaxis are set out. The latter include attention to personal clothing and undressing facilities, nutrition and cleanliness and annual holidays at no expense to the workers. Routine examination of workers is essential with special stress on urine examination every month, yearly cytological examination of urine by the method of Papanicolaou and cystoscopy only when urinary examination findings lead to the suspicion of a bladder tumour. *M. E. Delafield*

WOLKOWA, S. A. Die Bedeutung der Askorbinsäure bei Vergiftungen von Tieren mit Anilin bei hohen Lufttemperaturen. [**The Effect of Ascorbic Acid on Experimental Aniline Poisoning in Animals kept at High Atmospheric Temperatures**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 3, 375–82, 2 figs. [13 refs.]

The introduction to this paper contains references to the value of ascorbic acid in the treatment of a number of industrial poisonings such as those of carbon monoxide, lead, tetra-ethyl lead, benzol, carbon tetrachloride, aniline, dinitrophenol and cyanide. The mechanism of this therapeutic action is not yet understood fully. Some published work has shown that ascorbic acid hastens the excretion of para-aminophenol and of free and combined phenols by the urine in aniline poisoning. The author refers to his own observations on the effect of high temperatures 34–37°C. on aniline poisoning in increasing its severity and slowing up the conversion of aniline to para-aminophenol. These findings led to the experiments on rabbits and guineapigs described in this paper which had as their object the examination of the effect of ascorbic acid in aniline poisoning in the animals kept at a temperature of 35–37°C. (rabbits) or 32–36°C. (guineapigs). Details are given of the amounts of aniline and of ascorbic acid which were administered and of the analytical procedures used for the determination of the concentration of aniline in the blood and para-aminophenol in the blood and urine. Some determinations of the ascorbic acid content of the tissues of poisoned and control animals were also carried out. The rabbits were given a dose of aniline (100 mgm. per kgm.) intravenously after 3 weeks of pre-treatment with ascorbic acid and the experiment was only of short duration. The guineapigs after a month of ascorbic acid treatment were given aniline subcutaneously every second day and ascorbic acid daily during 3 months.

The results which are set out in figures and a table indicate that ascorbic acid improves the general condition of guineapigs with chronic aniline poisoning kept at a high temperature and also aids the conversion of aniline to para-aminophenol and accelerates the urinary excretion of para-aminophenol in both rabbits and guineapigs. *M. E. Delafield*

CHALLEN, P. J. R. HICKISH, D. E. & BEDFORD, Joan. **Chronic Chloroform Intoxication.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 243–9, 2 figs. [15 refs.]

The authors briefly review the toxicity of chloroform and its use in industry. The investigation centres on a firm making lozenges, one of the main ingredients being chloroform.

After the formula is mixed in a closed process the moist paste is discharged on an open tray, covered with a damp cloth and removed to the cutting room. It was here that the operators complained of the vapours given off during cutting and hardening.

The air sampling techniques are described and results tabulated. 22 women (8 long-service, 9 short-service, and 5 controls) were medically examined. Sleepiness, flatulence, tight feeling in the chest, nausea, frequency of micturition and mental slowness were some of the symptoms complained of by those long exposed. Several of the short-service workers, but none of the controls, complained of similar symptoms. The concentrations of chloroform of the more heavily exposed group varied from 77 to 237 p.p.m. and 9 out of 10 of these complained of severe symptoms. No evidence of liver damage was discovered in 8 workers who submitted to liver function tests.

The authors conclude that the maximum allowable concentration of 100 p.p.m. recommended by the American Conference of Governmental Industrial Hygienists is considered to be too high, and the evidence from the present investigation supports the value of 50 p.p.m. suggested by Imperial Chemical Industries Ltd. *T. O. Garland*

DEICHMANN, W. B., KEPLINGER, M. L. & LANIER, G. E. **Acute Effects of Nitro-Olefins upon Experimental Animals. Preliminary Report.** *Arch. Indust. Health.* Chicago. 1958, Oct., v. 18, No. 4, 312–19, 4 figs.

Among the hydrocarbons in automobile exhaust gases are olefins which combine with nitrogen oxides to form nitro-olefins. These are related to the prevalence of smog in Los Angeles, and are said to cause smog plant damage in concentrations as low as 0·2 to 0·5 p.p.m. The compounds are very volatile and are rapidly absorbed through skin.

Studies were made on rats, chicks and rabbits. Regardless of the route of administration all nitro-olefins elicited broadly similar toxic effects, namely: irritation of the eyes with inflammation of conjunctiva and eyelids; peripheral vasodilatation (red ears, nose

and paws); irritation of respiratory tract with excretion of mucous; tachycardia; tremors; and finally cyanosis, coma, asphyxial convulsions and death. Apart from the general toxic effect marked local changes are produced in the skin or enteric tract according to mode of administration. Pathological changes are described and illustrated. *T. O. Garland*

FAIRCHILD, E. J. & STOKINGER, H. E. **Toxicologic Studies on Organic Sulphur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans).** *Amer. Indust. Hyg. Ass. J.* 1958, June, v. 19, No. 3, 171–89, 2 figs. [35 refs.]

Organic sulphur compounds are constituents of petroleum and an increasing number of them are being discovered and used in industry. The presence of sulphur compounds other than sulphur dioxide and hydrogen sulphide in the atmosphere as contaminants in certain types of air pollution have, until very recently, received but little attention. No information is available on the exact nature of materials in refinery emissions. In addition to small amounts of particulate matter, NO_2, CO and hydrocarbons, sulphur compounds occur, presumably consisting of predominantly low-boiling, stable thiols and sulphides, as well as H_2S and SO_2. Other sources of atmospheric contamination by sulphur compounds, possibly some organic, are paper mills, zinc plants, lead, copper and nickel smelters, and coal combustion. Fumes from burning fuel oil and gas, motor exhaust fumes and photochemical synthesis cannot be overlooked as possible sources of organic sulphur compounds. There is little information in the literature on acute and chronic thiol toxicity and that which is reported is often conflicting. Data are likewise meagre regarding thiol toxicity in man. The authors have conducted animal toxicity studies of the following compounds: ethanethiol, 1-propanethiol, 2-methyl-1-propanethiol, 2-methyl-2-propanethiol, 1-butanethiol, 1-hexanethiol, methyl hepatanethiol, benzene thiol and α-toluene thiol. This is a lengthy communication and difficult to do justice to in an abstract. The interested reader will find ample detail concerning the experimental methods and the results in the original.

The degree of toxicity was rated on the results obtained for all routes of administration. Benzenethiol and methyl heptanethiol were found to have a high degree of toxicity and lethality, 2-methyl-2-propanethiol and 2-methyl-1-propane-thiol were considered relatively nontoxic, and the remainder ranged from moderately toxic to slightly toxic. Thiols had the common toxicological property of being soporific, the degree ranging from mild stupor to heavy sedation. Methyl heptane-thiol was an exception, producing a powerful central nervous system [CNS] stimulatory effect. Significant amounts of thiols were eliminated in the expired air of animals dosed by all but the ocular route. Thus, pulmonary elimination of thiols was a factor of importance in determining ultimate toxicity of these materials. Acute thiol poisoning produced a uniform pattern of central depression and respiratory paralysis with death ensuing from respiratory failure. Methyl heptanethiol, on the other hand, was typical of well-known CNS stimulants such as picrotoxin and pentylenetetrazol, having an analeptic action on the higher CNS centres and producing motor, respiratory, and vasomotor stimulation in relatively small doses. It was shown to counteract the central depression induced by barbiturates. Splenic enlargement was the only gross pathological change produced with consistency. Benzenethiol produced injury to the cornea and conjunctivae of rabbits. Thiol-exposed rats and mice commonly showed either latent pulmonary infection or pneumonia or both.

Personnel handling thiols under circumstances which might involve spillage should be warned against breathing the contaminated atmosphere for prolonged periods; this recommendation holds specially for benzenethiol and methyl heptanethiol. The toxic effects of the latter substances by the cutaneous route further emphasize the need for exercizing care in handling in order to avoid spillage and subsequent contamination. Contaminated eyes should be washed thoroughly and promptly with a weak silver nitrate solution (0·5%) or some other complexing agent and then flushed with copious amounts of water. The rationale in emergency treatment of general thiol intoxication indicates the usual supportive therapy for terminating the effects of central depressants, *e.g.* maintenance of a patent airway, the administration of oxygen or the use of artificial respiration of both. Analeptic agents may be of some value in counteracting the toxic action of thiols, but are obviously contra-indicated for CNS stimulants such as methyl heptanethiol.

The authors conclude that the potential hazards of benzenethiol and methyl heptanethiol as air pollutants would appear significant not only because of their intrinsic high toxicity, but also for their as yet unknown cumulative effects at air pollution levels.

P. J. R. Challen

DUNLAP, M. K., KODAMA, J. K., WELLINGTON, J. S., ANDERSON, H. H. & HINE, C. H. **The Toxicity of Allyl Alcohol. I. Acute and Chronic Toxicity.** *Arch. Indust. Health.* Chicago. 1958, Oct., v. 18, No. 4, 303–11. [17 refs.]

Allyl alcohol and its derivatives are widely used in chemical, resin and pharmaceutical manufacture. Originally it aroused interest as a contaminant of methyl alcohol used for denaturing ethyl alcohol. The present paper gives the results of primary irritation studies on rabbits, acute toxicity studies on rats, mice and rabbits, and sensory threshold studies on human volunteers.

When administered to rodents the outstanding sign was apathy preceded in mice by excitability, in rats by anxiety and in rabbits by bellicosity. A concentration of 150 p.p.m. proved highly lethal. Diarrhoea, convulsions or coma occurred sometimes before death.

The gross post-mortem findings were oedema of the lungs and engorgement of other viscera, while microscopically there were various signs of damage to the liver, kidneys and enteric tract. Lesions were similar at 100, 60 and 40 p.p.m. but less intense, the most persistent sign being eye discharge. Below these concentrations signs of irritation disappeared.

Few signs of abnormality were observed during the chronic ingestion studies.

In the study of sensory response by human beings eye irritation occurred in concentrations above 25 p.p.m. and nose irritation was noticed by 4 out of 7 subjects at 12·5 p.p.m. The suggested threshold limit is 10 p.p.m.

No evidence of liver damage or disturbed kidney function has been noted in persons occasionally exposed to this alcohol over a 10-year period. Its potency as a lachrymator provides warning of its presence.

T. O. Garland

CHALLEN, P. J. R., HICKISH, D. E. & BEDFORD, Joan. **An Investigation of some Health Hazards in an Inert-Gas Tungsten-Arc Welding Shop.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 276–82, 4 figs.

The authors give a clear, concise description of argon arc welding, why this technique is so useful for aluminium work and how ozone comes to be liberated during the process.

The firm investigated was manufacturing aluminium milk churns, and the sister in the medical department noticed the frequency of complaints of upper respiratory symptoms among the welders. Before welding the parts are degreased in trichlorethylene.

Analysis of air around the welders gave concentrations of ozone up to 1·07 p.p.m. and up to 69 p.p.m. of trichlorethylene. Virtually no phosgene was found. Full details of sampling techniques are described and the results are summarized in a table.

14 employees (11 female, 3 male) who were exposed were interviewed and 2 case histories are given in detail. Only 3 of the 14 were free from symptoms, others complained of dry mouth and throat, irritation of nose and lachrymation, and nasty smell. 5 were subject to diurnal lassitude and 2 to feelings of substernal oppression.

There is a short discussion on the dangers of ozone and finally a description of the control methods adopted. No further symptoms were reported after ozone concentrations were reduced to the region of 0·2 p.p.m., thus supporting the decision of the American Conference of Governmental Industrial Hygienists (1956) to lower the maximum allowable concentration for ozone from 1·0 to 0·1 p.p.m. *T. O. Garland*

DALHAMN, T. & GERHARDSSON, G. Ozon. En yrkeshygienisk och toxikologisk undersökning. [**A Hygienic and Toxicological Study of Ozone**] *Nordisk Hyg. Tidskr.* 1958, v. 39, Nos. 9/10, 145–64, 7 figs. [31 refs.]

The English summary appended to the paper is as follows:—

"The concentration of ozone and of nitrous gases was measured in a number of electric generating plants. In plants with open cooling systems low ozone concentrations (<0·07 ppm) were found, while in plants with closed cooling systems, particularly in the generator chambers, the ozone concentrations frequently were considerably higher (maximally 3·7 ppm). The tests concerning nitrous gases showed that these did not constitute a hygienic problem in the generating plants.

"The biologic effect of ozone was examined by allowing rats to run freely in an ozone-containing atmosphere (3·7 ppm) and also by observing the action of ozone on the movements of the tracheal cilia in rats. Histologic study of many organs following the former tests yielded largely normal findings. Nor was there any discernible effect on ciliary activity."

CONLEY, B. E. **Morbidity and Mortality from Economic Poisons in the United States.** *Arch. Indust. Health.* Chicago. 1958, Aug., v. 18, No. 2, 126–33, 4 figs.

"In the period 1948–1950, the first organized efforts were made to record exclusively occupational and other types of illnesses attributable to economic poisons." The Committee on Pesticides of the American Medical Association and the California Bureau of Adult Health began to collect and summarize case histories of pesticide poisoning. The progress of this work is continuing and a great deal of information has been obtained from many sources, although it was found that over half of the states and territories and three-quarters of the large cities had no pesticide poisoning records.

In this paper it is pointed out that the national vital statistics of the United States give mortality figures; for example that 8,000 persons lost their lives from accidental and intentional over-exposure to harmful chemicals in 1955, but that death records alone do not give the picture of the total of fatal and non-fatal poisonings. Collection of case histories of pesticides poisonings such as those which have been described is of much value. The data thus obtained are briefly but effectively analysed and reviewed. There is also a table which sets out the accidental deaths from each of a number of different insecticides and rodenticides in the United States yearly in the period 1946–55.

M. E. Delafield

MINISTRY OF AGRICULTURE, FISHERIES AND FOOD. **Use of Sodium Fluoracetate as a Rodenticide. Precautionary Measures.** 4 pp. 1958, Sept. London: H.M. Stationery Office. [4d.].

This is a short, clearly written leaflet on the precautionary measures which should be adopted in the use of sodium fluoracetate (sometimes referred to as "1080" or more correctly as sodium monofluoracetate). This substance is a very useful and effective rodenticide, but the chemical and the baits made up from it are more toxic than most other rodenticides and must therefore be used with more care. There are 27 short paragraphs, none of which is more than a few lines long, which give information about the properties of the chemical, its toxic effects, the immediate treatment in cases of poisoning and the precautions to be taken in its use. These precautions are stated under the headings of: supply and sale of the poison, handling the chemical and making up baits, handling and laying of made-up bait, location of baiting points, and removing baits and clearing up after treatments. *M. E. Delafield*

MENON, J. A. **Tropical Hazards associated with the Use of Pentachlorophenol.** *Brit. Med. J.* 1958, May 17, 1156–8. [10 refs.]

Sodium pentachlorophenate (Santobrite) is used as a preservative, fungicide and disinfectant for wood in Sarawak, especially to prevent "sap stains"; it is soluble in water. [It is also used as a molluscicide in the control of schistosomiasis.] It is not a scheduled poison, and its toxic effect is not clearly defined, but the author reports 9 deaths within a period of 15 months in Dyak workmen engaged in dipping timber in a tank of pentachlorophenate solution and handling the wet wood after withdrawal.

The symptoms of poisoning came on quickly in all cases, and death took place within 9–25 hours. Hyperpyrexia (to 108°F. in 1 instance), gross dyspnoea and prolific sweating were all noted, and spasm was common [but is not described in detail]. Treatment was unsatisfactory, comprising measures to combat the hyperpyrexia, to replace electrolytes and glucose destroyed as a result of the high basal metabolic rate induced by the pentachlorophenate. The author suggests that cortisone and chlorpromazine might be useful.

The findings at autopsy were not helpful, and chemical analysis of the organs of 7 subjects was negative. Pentachlorophenate was found in the urine of 1 of 3 men so examined.

The author concludes that "there would seem little doubt that the nine patients died of intoxication with pentachlorophenol", and stresses the importance of using rubber gloves, aprons and boots, of the provision of washing facilities for the workmen, and of restricting this work to periods of not more than 14 days at a time.

Curiously enough, Chinese workmen doing the same work have not been similarly affected.

[The author does not give the strength of the labour force, and it is therefore not possible to assess the frequency of this condition, but it is obviously one which needs investigation.] *Charles Wilcocks*

BRZOZOWSKI, J., BERBEC, W., RODZIEWICZ, J. & WÓJCIK, J. Higiena pracy i stan zdrowia zatrudnionych podczas niszczenia stonki ziemniaczanej dwuchloroetanem. [**Hygiene of Work and State of Health of Workers employed in destroying the Colorado Beetle with Dichlorethane**] *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1957, v. 12, 281–94, 2 figs. [23 refs.]

The English summary appended to the paper is as follows:—

"In order to answer the question how far dichlorethane can endanger the health of worker employed in destroying the Colorado beetle, and what prophylactic measures should be used, the Institute of Rural Medicine and Hygiene carried out field investigations in the years 1953—1954. Investigations concerning the conditions of work consisted among others in determining the level of dichlorethane in the air. The examination of the state of health of 118 workers consisted in: medical examination in the out-patient department (internal and dermatological), clinical examination (some patients), haemoglobin estimation in blood, numerical count of cells, differential leucocytic count, urinanalysis comprising estimation of dichlorethane level, and in epidermal tests according to Jadassohn-Bloch. The results were analysed statistically.

"The investigations showed that the danger of absorbing dichlorethane by inhalation was slight. On the other hand, careless handling of the preparation could facilitate its absorption through skin, and this situation might be still aggravated by the unfavourable influence of changing atmospheric conditions and inadequate diet.

"No cases of acute poisoning were observed, but about 10 per cent of the examined workers showed changes caused by dichlorethane justifying the need of interrupting their contact with the preparation in order to prevent a more serious impairment of health.

"In 18 per cent of the examined workers there was found an increased haemoglobin level in blood, in 75 per cent a decreased number of neutrophils, and in 90 per cent an increased number of lymphocytes. The results of haematological investigations (which are at variance with those to be found in literature) can be explained by the short time of exposition of the examined persons. In conclusion, the authors indicate practical means for improving the sanitary conditions of the work.

"A mention must be made of an unsuccessful attempt at testing in out-patient department conditions the liver function by means of Quick's hippuric method. The introdution of periodical functional liver tests which might be useful in such condition requires further theoretical consideration in view of the disintoxicating function of the liver."

BELL, A. & JONES, A. T. **Fumigation with Dichlorethyl Ether and Chlordane: Hysterical Sequelae.** *Med. J. Australia.* 1958, Aug. 23, v. 2, No. 8, 258–63, 1 figs. [14 refs.]

On account of borer infestation 60 gallons of a mixture of 12% dichlorethyl ether and 2% chlordane dissolved in kerosene were sprayed on to the wooden foundation beams of a clothing factory. The operator completed spraying between June 21 and June 25, 1956 and he himself remained well. On June 25 a girl aged 19 complained of a mild skin irritation of chest and face and later fainted. A few hours later 2 more girls, and within 5 or 6 days 12 more employees, were similarly affected. At this stage the management closed the factory, but cases continued to occur for a week. In all, 55 employees out of a total of 166 were ill, all of them relatively mildly.

On July 6 an industrial hygiene team visited the factory. Tests revealed no carbon monoxide in the air and no trace of chlorinated hydrocarbons. Only a faint smell of kerosene was noticed.

Further tests revealed that it was possible that enough vapour from the spray might have been present in the work rooms to cause some slight irritation of skin and mucous membranes during the first day or two. However, the argument is developed and in a convincing manner, that mass hysteria among the girls was the cause of the absenteeism. *T. O. Garland*

ORTELEE, M. F. **Study of Men with prolonged Intensive Occupational Exposure to DDT.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 433–40, 1 fig. [24 refs.]

40 men were studied, all employed by firms manufacturing very large amounts of DDT. Exposures were mainly dermal (very heavy) and respiratory with a small amount of ingested DDT from smoking on the job and from dust settling in mouth and nose. No protective clothing or respirators were in use.

Clinical and laboratory tests are described. They included estimation of plasma and erythrocyte cholinesterase and DDA excretion. The latter test makes it possible to calculate DDT absorbtion.

The only correlation found with high exposure was increased DDA excretion and a few cases of mild skin and eye irritation. The mild skin rashes subsided spontaneously in spite of continued exposure. The eye irritation was no more severe than might be experienced from a heavy concentration of any kind of dust.

It is comforting to have these findings recorded for most samples of human fat and milk in the U.S.A. now contain detectable amounts of DDT of dietary origin. *T. O. Garland*

VARGAS, L., GARZA DE LOS SANTOS, A. & COLORADO IRIS, R. Observaciones sobre la toxicidad de la Dieldrina, insecticida usado para erradicar al paludismo. [**Observations on the Toxicity of Dieldrin**] *Gac. Méd. de México.* 1957, May, v. 87, No. 5, 345–56.

Experiments on rats and guineapigs indicated that the toxicity of dieldrin (LD50) when given by mouth was about 0·046 and 0·04 gm. per kgm. respectively.

The symptoms produced in animals by a toxic dose are similar to those produced by the organic phosphates; they are increased by prostigmin and acetylcholine and reduced by atropine. For treatment, therefore, atropine should be used, but its action appears to be transient, and it was not found effective in prevention when given ½ hour before administration of dieldrin. The recommended dose of atropine for animals poisoned with dieldrin is about 0·0005 gm. per kgm., and for a synthetic derivation of papaverine 0·017 gm. per kgm.; these are maximal doses.

Anopheles aztecus and *A. albimanus* were very susceptible to dieldrin in the blood of animals on which they fed. *Charles Wilcocks*

CULVER, D., KINOSIAN, J., THIELEN, W. & GRAUL, R. **A Study of Exposure to Parathion in a Greenhouse.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, No. 3, 235–47, 6 figs.

Studies were made on 11 employees working in greenhouses in California. Exposures to parathion were estimated and cholinesterase levels in the workers were recorded twice a week. Details of spraying, sampling and analytical techniques are recorded in minute detail.

There was no evidence of any parathion vapour present after the mist had settled, *i.e.* within 1½ hours or less. Workers were not allowed to return to work in a house until the third day after spraying.

There is no method for estimating skin absorption. Watering bean plants and handling small tomato plants resulted in a small accumulation of parathion on hands —tying and crossing pea plants resulted in greater contamination. Cholinesterase determinations showed no apparent relationship to periods of high surface residue on plants or to long hours of exposure, but a depression of cholinesterase levels did occur.

Most workers smoked while handling plants. This should be avoided. Protective clothing and good housekeeping and careful medical supervision is required. *T. O. Garland*

ARCH. INDUST. HEALTH. Chicago. 1958, Nov., v. 18, No. 5, 441–5, 2 figs. [13 refs.] **The Effect of Parathion on Human Red Blood Cell and Plasma Cholinesterase. Section I** [WILLIAMS, M. W., COOK, J. W., BLAKE, Jane R., JORGENSEN, P. S. & FRAWLEY, J. P.] **Section II** [RIDER, J. A., MOELLER, H. C., SWADER, Joyce & WEILERSTEIN, R. W.].

"Four male and four female volunteer subjects in good health were fed four levels of parathion for 12 weeks at 3 weeks per level. The successive dosages, which were fed daily as corn oil dilutions by capsule, were 0.003, 0.010, 0.025, and 0.050 mg/kg. of body weight. Two additional subjects were given corn oil placebos. Studies of the plasma and red cell cholinesterase levels by the method of Michel were made before, during, and after the feeding period. A significant increase in the mean plasma cholinesterase without an accompanying change in the red cell enzyme occurred early in the feeding program, but the levels declined to control values when doses of 0·050 mg/kg. were instituted. Upon completion of the feeding program a slight rebound in the mean plasma cholinesterase was noted. Mean control levels did not change significantly throughout the study.

"It is concluded that the daily ingestion of 0.050 mg/kg. of parathion for a period of three weeks produces no decrease in human plasma or red cell cholinesterase activity, while lower dosages induce some increase in the plasma cholinesterase level."

SWANN, H. E., Jr., WOODSON, G. S. & BALLARD, T. A. **The Acute Toxicity of Intramuscular Parathion in Rats and the relation of Weight, Sex and Sex Hormones to this Toxicity.** *Amer. Indust. Hyg. Ass. J.* 1958, June, v. 19, No. 3, 190–95, 3 figs. [14 refs.]

Many studies of parathion toxicity have been made on the rat. These have included acute and chronic values for parathion by oral, intraperitoneal, intravenous and dermal administration, but no intramuscular studies have been reported. The latter could be of value, because parathion is rapidly absorbed and highly toxic by dermal application, and intramuscular injection might be a means of quantitating dermal absorption. In addition, the literature does not contain any studies of intravenous, dermal or intramuscular

administration of parathion where comparisons were made between the sexes. The female rat was found to be more susceptible than the male when parathion was administered by the oral or intraperitoneal route.

The authors have carried out experiments to establish the intramuscular LD50 for young mature (140–220 gm.) male and female rats, and to ascertain whether there is any difference in the susceptibility to parathion for rats of different weights.

Parathion inhibits cholinesterase and investigators have tried to demonstrate a relationship between the activity or the inhibition of the enzyme and the sex of the animal.

Dubois *et al.* [this *Bulletin*, 1949, v. 24, 426] injected male and female rats with the opposite hormones and reported that this tended to equalize their susceptibility to parathion. These experiments have been repeated by the authors. Their experimental methods and results are presented in detail in the original.

The intramuscular LD50 to parathion for the young mature female and male rat are respectively given as 10·4 mgm. per kgm. and 41·4 mgm per kgm. At other weights the immature males and all females have approximately equal values, while the mature male values are high. It is concluded from these results that the male obtains added protection to the toxicity of parathion when sexual maturity is reached. In order to determine what effect the sex hormones have on the toxicity of parathion, intramuscular injections of the same and opposite sex hormones have been made into normal rats and rats with castration or ovariectomy. The results of these experiments indicate that injected testosterone propionate offers protection to the female rat, to the castrated male and to the female with ovariectomy. The injection of oestrone into the male decreases his protection. Castration of the male also decreases his protection and the injection of female hormone into the castrate causes further loss of protection.

The authors conclude that the male sex hormone appears to have a major role in the added protection of the mature male rat to the toxicity of parathion and that this phenomenon may be related to the level of androgen in the blood. *P. J. R. Challen*

O'Brien, R. D. & Davison, A. N. **Antagonists to Schradan Poisoning in Mice.** *Canadian J. Biochem. & Physiol.* 1958, Nov., v. 36, No. 11, 1203–10, 1 fig. [23 refs.]

"Twelve agents have been tested for their capacity to antagonize schradan poisoning. Three showed promise, and were examined in more detail. The best compound, SKF525A, confers protection even if given after the schradan. When given simultaneously, 20 mg/kg of SKF525A raises the LD_{50} of schradan from 21 to about 80 mg/kg. There are two optima in the treatment times with SKF525A: at 1 hour before and simultaneously with the schradan. SKF525A also has a protective action against other compounds, notably Guthion, yet is without effect on parathion poisoning. The order of effectiveness of SKF525A, iproniazid, and 3-acetylpyridine in antagonizing schradan poisoning closely parallels their order of effectiveness in antagonizing pentobarbital detoxification; the significance of this is discussed. The protection afforded by these agents is probably due to inhibition of the activation of phosphorothionates and phosphoroamidates."

Bordás, S., Kanyó, B., Nagy, Mária E. & Weber, Teréz. A Wofatox—és Malathionpermetezés expozíciós vizsgálata. [**Study of Exposure to Wofatox and Malathion Through Spraying**] *Egészségtudomány.* Budapest. 1958, v. 2, No. 1, 56–73, 1 fig. [32 refs.] German summary.

In an investigation of the toxicity of the cholinesterase-inhibiting insecticides malathion (S-1:2-dicarboxyethyl-OO-dimethyldithiophosphate) and Wofatox [methyl parathion] (OO-dimethyl-O-*p*-nitrophenylthiophosphate) under practical conditions determinations were made of the content of the preparations in air samples and on clothing of workers during the course of spraying operations in orchards. Air concentrations of malathion of 0·5–1·0 mgm. per cu. m. were observed during hand and motor spraying; although contamination of the clothing reached the maximum level permitted, no fall of serum pseudocholinesterase activity was observed after spraying throughout 1–3 working days, and it is concluded that protective clothing is not necessary. During the spraying of sugar beet with Wofatox air concentrations of 0·75–1·35 mgm. per cu. m. were recorded in the neighbourhood of the operator. No signs of intoxication or fall in serum pseudocholinesterase activity were observed after a 48-hour week in operators who wore protective clothing continuously, but wore gloves and gas masks only during visible exposure to spray.

D. J. Bauer

Bruaux, P. Toxicité de deux insecticides organophosphorés (Diazinon et Malathion) chez les travailleurs utilisant ces insecticides. [**Toxicity of 2 Organic Phosphate Insecticides (Diazinon and Malathion) in Workmen handling them**] *Ann. Soc. Belge de Méd. Trop.* 1957, Dec. 31, v. 37, No. 6, 789–99.

These and similar insecticides are likely to be used for control of human disease vectors and in agriculture; the author therefore, in Léopoldville, investigated their action in workmen handling them. The chief hazard is through skin absorption, and there is normally little risk of ingestion or inhalation; workmen should therefore carefully wash their hands and other exposed parts of the skin, at the end of the work, and should wear special protective clothing. The early symptoms of intoxication are not characteristic—headache, nausea, fatigue—but later symptoms may include miosis, vomiting, diarrhoea and convulsions.

Normal cholinesterase values were calculated for plasma and erythrocytes in 74 unexposed workmen. In 36 men handling Diazinon the average value for plasma immediately after 2 years of contact with the insecticide was considerably below normal, but had returned to normal 1½ months later. For erythrocytes no deviation from normal was found.

Malathion is more toxic than Diazinon, but in 36 workmen, after 1 year of exposure, the average plasma cholinesterase was normal though there was slight reduction in erythrocyte cholinesterase.

The average figures are given, but the author remarks that in some individual instances the reduction in cholinesterase (down to 20% of normal) reached potentially dangerous levels, though none of the men had symptoms of intoxication. Nevertheless, in hot countries the recommended precautions are not easy to take, and the risk is correspondingly increased; supervision should therefore be specially strict.

Charles Wilcocks

BUCKLEY, W. R. **Lichenoid Eruptions following Contact Dermatitis.** *Arch. Dermat.* 1958, Oct., v. 78, No. 4, 454–7, 9 coloured figs. on pl.

Lichen-planus-like reactions to parenteral gold, ingested mepacrine, and an astonishing variety of other drugs are familiar to all, but this seems to be the first report of lichenoid eruptions by contact.

The author, consultant in dermatology to the Eastman Kodak Co. of Rochester N.Y., to whom an incidence of 25% among workers exposed to paraphenylenediamine in photographic processes had been reported by a colleague, does not tell us how many of these cases he has seen himself. But what he describes should be an easily recognizable clinical picture. He tells us that the familiar type of acute allergic reaction to paraphenylenediamine is seen initially in only 10% of his cases. The acute reaction may undergo lichenoid evolution and the subacute one described here may become eczematoid. The characteristic picture of this subacute reaction to paraphenylenediamine consists of loss of eponychial tissue and a reddish purple discoloration of the distal dorsal phalanges "with occasionally petechiae at the tips of the fingers". With all the resources of the Eastman organization at his disposal it is disappointing that he cannot name a hue with greater precision than "reddish purple" or "violaceous" [which is of course, for dermatologists, tautological of lichen planus]; but the colour photograph helps us to see that the dorsal aspect of the phalanges is discoloured but without the sort of emphasis on the skin folds around the nail that we see in "tulip fingers" and might perhaps understand by "loss of eponychial tissue". With further exposure there may be a confluent violaceous oedematous papular response in the interdigital webs (not clearly shown in the photograph) and on the flexor aspect of the wrists spreading to the forearms. The face is spared but the pattern of generalization includes not only scattered lichen planus papules but also an eczematoid response on the sides of the neck and antecubital flexures. Neither mucous membrane lesions nor any systemic reaction has been noted. The histology may or may not closely resemble that of lichen planus. Healing follows abstention from contact and is accompanied by pigmentation of the lesions. Palmar hyperhidrosis is mentioned as a sequel of the disease.

The author gives good reasons for not regarding it as a Köbner provocation of spontaneous lichen planus. He states but fails to show pictorially that positive patch tests undergo lichenoid evolution.

He makes no comment on the sudden appearance in epidemic form of a type of reaction not hitherto associated with cutaneous sensitization.

J. H. Twiston Davies

RAMOS E SILVA, J. & COZZOLINO, D. Algumas observações de uma dermatose profissional "sui-generis": a tilose subungueal. [**Observations on an Occupational Dermatosis. Subungual Tylosis**] *Rev. Assoc. Méd. Minas Gerais.* 1957, Sept.–Dec., v. 8, Nos. 3/4, 141–4, 4 figs.

The English summary appended to the paper is as follows:—

"1. Forty-one workers of one tanyard and two laundries who showed peculiar lesions of the finger-tips were studied.

"2. The lesions were essentially by a marked and circumscribed thickening of the epidermis, mainly in the stratum corneum. The thickening forms a hard and elevated fringe under the free margin of the nail, between this part of the nail and the digital pulp.

"3. The name *professional sub-ungual tylosis* is proposed by the authors for this particular lesion.

"4. Side-manifestations in these cases are: onycholysis, trachyonyxis, thickening of the ungual plate, maceration and exfoliation of the epidermis of the neighbourhood.

"5. The lesions are mainly of mechanical origin, resulting from the nature of the work; secondarily, the humidity and the action of irritating chemicals are contributory factors."

ZUPPINGER, A. Die Gefährdung durch ionisierende Strahlungen. [**The Danger from Ionizing Radiation**] *Schweiz. med. Woch.* 1958, Nov. 22, v. 88, No. 47, 1171–9, 2 figs. [Numerous refs.]

The author has written a comprehensive account of the various ways in which man is nowadays subject to the hazards of irradiation; these ways are numerous, beginning with the natural irradiation conditions for all living things on earth, then on to the man-made irradiation complex ranging on the one side from nuclear power dangers to those brought into play in medical radiology, especially radio-diagnosis. The author goes into great detail in the last respect and he has grouped together in Tables I and II a large number of data showing the doses received by the gonads of patients, male and female, during radio-diagnostic examinations; we learn from this that in females the largest dose to the gonads occurs in hysterosalpinography, whereas in males it occurs in urethrocystography. A very wide range of dosage occurs in radio-diagnosis of the various parts of the body, and it is doubtful whether somatic, in contrast to genetic, damage is at all a common feature with present-day techniques.

The author discusses prophylaxis and treatment of radiation damage. Considerable attention is paid by him to the counteraction of such damage by chemical

means, although he concedes that the whole of the subject is very undeveloped.

The author has drawn up a set of conclusions on the whole question of radiation damage, 22 in number. Most of these recommendations of safety have appeared in the literature since 1945 and gained general acceptance, but special mention may be made here of the claim that somatic damage by the rays is to be feared above all for its late effects. The author finds that blood counts are useless as indicators of minor radiation damage. In man total exposure of 200γ is said to increase the expectancy of leukaemia 10-fold; many will consider this an over-bold statement as the production of leukaemia by X-rays is still in dispute. Damage to the embryo is most likely in the first 2 months of pregnancy, hence the need for special care in pelvic X-ray examinations; there must be a very real need for their justification.

This is a valuable article on a subject whose significance seems to increase every year.

S. Russ

COGAN, D. G., FRICKER, S. J., LUBIN, M., DONALDSON, D. D. & HARDY, Harriet. **Cataracts and Ultra-High-Frequency Radiation.** *Arch. Indust. Health.* Chicago. 1958, Oct., v. 18, No. 4, 299–302.

In radar and communications installations increasing amounts of power are being used, and as a result persons may be exposed to larger doses of radiation of radio-frequencies varying probably from the ultra-high-frequency band, at a few hundred megacycles a second, to the microwave band at several thousand megacycles a second. Intense microwave radiation applied locally to the eyes has produced cataract in animals. The study described here was made to determine whether or not cataracts might result from exposure of the whole body to radiation at frequencies similar to those used in some high-power installations—frequencies of the order of 400 megacycles.

The experimental techniques employed are described in detail. Rabbits were used in these experiments, and most of the exposures were carried out in a wave-guide system so that measurements of the power absorbed, as well as of the field intensities, could be made.

Rabbits were repeatedly exposed to radiation at a frequency of 468 megacycles a second and an intensity of 60 mw. per sq. cm. for periods of 20 minutes. No cataracts developed after these repeated exposures to near-lethal doses of radiation. *Thomas Bedford*

See also p. 301, GERSTNER, **Acute Clinical Effects of Penetrating Nuclear Radiation.**

WILHELM, G. Die Strahlenbelastung im Kindesalter. [**Radiation Exposure in Childhood**] *Deut. med. Woch.* 1958, Sept. 12, v. 83, No. 37, 1618–23, 1639. [16 refs.]

The author is attached to the Universitäts-Kinderklinik in Frankfurt and the present article is a well documented plea for the fullest consideration of the danger that young children and those not yet born may be subject to from ionizing radiations—man-made as well as those provided by nature, *e.g.* natural radio-activity and cosmic radiation.

The chief sources of danger among the former arise from X-ray diagnoses; this is generally agreed by writers from many countries, and the author makes a strong plea that these diagnoses should be reduced to a minimum, not by any ruthless edicts but the strictest attention to their clinical necessity. There are 2 distinct categories here; one in which the expectant mother is examined by X-ray and the other in which the young child is exposed. Tabular data show that in both of these categories the X-ray doses given to the tissues may be of great importance.

Once again it is emphasized that doses of radiation are additive when the hereditary effects come into consideration. The somatic effects of doses of radiation spread over the years may well be tolerated by the individual; in fact the standpoint adopted in specifying permissible doses is founded upon this condition, but it is otherwise with action upon the gonads, for as far as we know there is no lower limit to the dose that can produce a mutation; unfortunately mutations induced by radiation are undesirable ones. Consequently the concern is now a world-wide one that future generations are not going to be handicapped by what we do to germ plasm in our own day.

The author is concerned also with the growing menace of radio-strontium from the fall-out that occurs after any atom bomb explosion. This material may hang about in the stratosphere or troposphere for a period of up to 10 years, gradually settling on the vegetation, then being ingested by cattle and finding its way to the population by the milk supply. All of the author's points are substantiated by tabular data drawn from numerous sources

[This is a paper that deserves to be widely read.]

S. Russ

STANNARD, J. N. **Dosage and Biological Effects of Internal Radioactivity.** *Arch. Indust. Health.* Chicago. 1958, Aug., v. 18, No. 2, 95–101, 1 fig. [15 refs.]

The author considers the factors for intelligent appraisal of the problems in handling radio-active materials. These fall into the categories external and internal hazards, of which the latter are probably now the more important. Whereas the former are hazards purely from radiation, the latter carry these as well as chemical toxicity; this is shown especially in dealing with uranium. The author usefully points out that there could be a radiation hazard to the lung from inhaled uranium dust even though insufficient amounts reach the kidney to cause significant chemical damage.

On p. 97 there is a calculation formula by which the dose to the body or any particular organ can be found, the necessary data having been established.

On permissible doses a distinction is drawn between those in which the practical level is arrived at from clinical experience, as is the case with radiation and those which are calculated from selected observation.

Reference is made to the information on these points in the *National Bureau of Standards Handbook 52*, U.S. DEPT. OF COMMERCE, March 1953. *S. Russ*

LAUGHLIN, J. S. **Dosage and Biological Effects of External Radiation Sources.** *Arch. Indust. Health.* Chicago. 1958, Aug., v. 18, No. 2, 102–5, 1 fig.

The author illustrates and describes a "phantom" of Presdwood (tissue equivalent) which may be taken to pieces and a skeleton introduced. Suitable measuring instruments can be inserted into any part of the body, *e.g.* bone marrow, ovary, testis etc. in order to find the relative doses they receive in diagnostic exposures. There are certain types of examinations which produce the most significant doses; they are intravenous and retrograde pyelography, urethral cystography, hip and femur, pelvimetry, obstetrical examinations, pelvis, lumbar spine and salpinography. All of these are examinations in which the gonads are either included in the direct beam or are sufficiently close to its path for the scattered radiation to be appreciable.

According to the author, the average dose to the gonads in radiotherapy is small compared with that occurring in diagnosis. [There are, however, likely to be exceptions to such a ruling; where a malignant growth is in question a risk to the gonads may have to be faced, bearing in mind greater risks which may face the therapist.] *S. Russ*

TEBROCK, H. E., YOUNG, W. N. & LOPEZ, H. **Clinical Approach and Laboratory Aids in Diagnosis and Treatment of Radiation Injury.** *Indust. Med. & Surgery.* Miami. 1958, Oct., v. 27, No. 10, 513–17.

This article is meant as an introduction to the physician of the clinical effects of ionizing radiation and how best to deal with them.

In the diagnosis of radiation injury, the authors maintain that the most important factor is the clinical history, especially regarding radiation exposure; once this is ascertained an attempt should be made to correlate the presenting signs and symptoms with the estimated radiation dose. The authors are especially insistent upon this when one has to deal with radiation burns. A patient in this category may in a few hours develop hyperaemia and oedema which last a few days; 3–4 weeks later he may have the appearance of second- and third-degree burns in the affected region, which slough and leave a poorly healing ulcer. After healing in 4 months the chronic phase of radiation burns occurs with dermatitis, epilation, keratoses and malignancies; the only reliable guide to prognosis in these cases is the dose of radiation received and the time over which it extended.

Dealing with delayed external radiation injury the authors maintain that the most striking feature is the damage to the integument of those injured; the genetic changes they regard as still a moot question and the undue incidence of leukaemia as still a matter of debate. They regard toxin formation as of little importance in the production of radiation illness. In the treatment of anyone acutely exposed, the primary aim must be to remove all contamination and check body surfaces with radiation counting devices. Removal of clothing and showering should be carried out promptly and the following routine is useful:—

(1) Clip and remove hair from the nose;
(2) sniff water up the nostril and expel through the mouth taking care not to swallow;
(3) if the water is swallowed, induce vomiting.

The whole paper is full of practical suggestions built on experience and could well be elaborated into a handy code of action. *S. Russ*

GARAVAGLIA, C., GHISLANDI, E. & POLVANI, C. Il servizio sanitario di un centro di ricerca nucleare applicata: scopo, organizzazione e metodi di lavoro. **[The Medical Service in a Centre of Applied Nuclear Research: Purposes, Organization and Working Methods]** *Med. d. Lavoro.* 1958, Oct., v. 49, No. 10, 572–90. [25 refs.]

The English summary appended to the paper is as follows:—

"In the introduction the Authors briefly recall that in a center of applied nuclear research there exist all possible types of occupational risk, deriving from ionizing radiations (external and internal irradiation; acute and chronic irradiation; irradiation of the whole body and of its individual parts). They then review the uncomplete national and international law provisions concerning the protection against ionizing radiation and examine successively the task, the organization and the working methods of the Medical Service (M.S.) of a nuclear center already operating in Italy for a number of years.

"Particularly, the position of the M.S. within the frame of the safety services of the center is emphasized, while its close collaboration and connections with the Health Physics Service (H.P.S.) are deeply examined. According to the Authors' opinion, in opposition to other solutions prevailing elsewhere, the M.S. and the H.P.S. have to be two independent and parallel services, acting jointly according to a by-law.

"As far as the structure of the M.S. is concerned, it differs in some measure from the conventional organization centered on the plant physician alone, since in this case particular and specialized knowledge is required. In the M.S. actually there must be one physician specialized in occupational medicine, who has the duties of plant physician, but is helped by a pathologist (who has the task of carrying out laboratory clinical investigations) and by a radiologist, having the functions of an adviser in the field of radiology and radiopathology.

"The working methods of such a group of physicians are described: the trends to be followed in the medical examinations are outlined, at the moment of the engagement as well as periodically; also the way of establishing the medical files is described. The medical files have, in-fact, to collect the results of the medical and laboratory examinations, the information concerning the working place and risks and the evaluation of the radiation doses absorbed by each worker.

"As regards the evaluation of the working conditions and of the absorbed doses, the Authors present a conventional 'code', defining and classifying respectively

occupational risks and absorbed doses, which may serve to rapidly transmit and interpret the results of the evaluations accomplished."

PARMEGGIANI, L. Preparazione di un progetto di regolamento del lavoro con le radiazioni ionizzanti. [**Preparation of Suggested Regulations for Work involving Ionizing Radiation**] *Med. d. Lavoro.* 1958, June–July, v. 49, Nos. 6/7, 457–68.

This paper contains in detail the draft proposals elaborated by the author and his colleagues to cover:—

1. General rules for industries which carry a radiation hazard.
2. Rules for the extraction of radio-active minerals.
3. Rules for the working of radio-active minerals.
4. Rules for the industrial use of X-rays and gamma radiation.

In these regulations physical control of the materials is stressed, and measures are suggested in outline for the protection of workers. *Charles Wilcocks*

Atmospheric Pollution

LOUISVILLE & JEFFERSON COUNTY. **The Air over Louisville. Summary of a Joint Report by the Special Air Pollution Study of Louisville and Jefferson County, Kentucky,** 1956–1957. 57 pp., numerous figs. 1958.

Although no catastrophic incident had occurred, concern was felt in Louisville at the growth of air pollution which accompanied post-war increases in population and industrial activity. City, county, state and federal authorities were mobilized and during 2 years carried out a scientific survey of the situation which is summarized in this attractively produced report. A more detailed technical report is being prepared and will be issued by the Community Air Pollution Program, U.S. Public Health Service, Cincinnati.

6 permanent sampling stations were set up, each equipped with 2 high-volume samplers alternating with one another to give continuous filtration of 25,000 cu. ft. of air per week. A low-volume tape sampler was also run at each station and gave a sequence of stains on a paper strip for measuring the soiling power of the atmosphere.

Samples were taken with mobile equipment in areas from which complaints had been received. Cascade impactors were used for air-borne particles, oiled glass slides for fall-out and various suction devices for gases. Meteorological observations on a considerable scale were maintained throughout the sampling period. The dispersion of stack effluents was studied by the introduction of powered zinc cadmium sulphide as a tracer, which fluoresced under ultra-violet light, and could be estimated on samples taken at various distances downwind.

Subjective perception of odour, gauged by a group of trained observers, deterioration of carbon steel springs and a bacteriological survey completed the programme of observations.

As a result of this activity it was demonstrated that some 440 tons of atmospheric pollutants were discharged daily over the city, of which 85% came from industry, 9% from domestic sources and 6% from vehicles. 90% of the pollution was particulate and 10% gaseous. Tables are given which show the main constituents of pollution from each of the 3 sources. Movement of pollution in relation to the weather is explained.

The report concludes with recommendations for action to be considered by the air pollution Control Board of the County. *C. N. Davies*

GOOSSENS, J. F. & LAFONTAINE, A. La pollution chimique de l'air dans les cités modernes et le probléme particulier des gaz de combustion des moteurs à explosions et des installations de chauffage. [**Chemical Air Pollution in Modern Cities and the Problem of Fumes from Internal Combustion Engines and Heating Installations**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1958, May, v. 16, No. 5, 217–37. [52 refs.]

In this paper the authors have reviewed in general terms the problem of atmospheric pollution in towns, paying particular attention to exhaust fumes from petrol and diesel engines.

Air contaminants are discussed under 3 headings—(a) industrial and domestic sources; (b) radio-active material from nuclear test explosions and from nuclear power stations; (c) carcinogenic substances, notably 3,4 benzpyrene and metallic contaminants such as arsenic, beryllium, chrome and nickel.

In air samples from the streets of Brussels the authors found the average concentration of carbon monoxide (CO) to be 10 p.p.m. Their results agreed with similar findings in Paris (CAMBIER and MAREY) but the authors point out that in the latter investigation the air in some thoroughfares had a concentration of 100 p.p.m. of carbon monoxide and in one instance the figure was 500 p.p.m. (MAC 100 p.p.m.).

Although DETTLING found 5 mgm. of lead per cubic metre of exhaust fumes at source when tetra-ethyl lead had been added to petrol, the general level of lead in the air of Cincinnati [this *Bulletin*, 1953 v. 28, 360] was found to vary from 0·1 μgm. to 12 μgm. per cubic

metre, this being very much below the maximum allowable concentration which has been given as 150 μgm. per cubic metre.

The authors go on to describe the irritant effects of sulphur dioxide (SO_2) and refer to the smogs of Los Angeles and London and other places. They point out the importance of the psychological effects of persistent smog, and suggest that the increased absorption of ultra-violet light under these conditions may contribute to a reduction in resistance to infection.

The composition of exhaust fumes from petrol and diesel engines is dealt with in some detail and interested readers are referred to the original article. The importance of good maintenance of motor-vehicle engines is stressed.

The authors then make a number of suggestions for reducing atmospheric pollution from these sources, among them being more attention to engine design, more research on fuels and better traffic planning to keep vehicles moving steadily with less stopping and starting.

An excellent bibliography is given and finally a table of maximum allowable concentrations of toxic substances. *F. G. M. Seager*

Physiology as Applied to Hygiene

LOEWENTHAL, L. J. A. & FREED, C. C. **Disturbances of Sweat Delivery in Deep-Level Gold Mines.** *Proc. Mine Med. Officers' Ass.* Johannesburg. 1958, May–June, v. 38, No. 364, 1–5. [16 refs.] Discussion 5–9.

The authors discuss prickly heat (miliaria rubra) and the factors that may contribute to its causation. Prickly heat occurs in the gold mines of South Africa, and its incidence increases with increasing depth of the works as the temperature and humidity rise.

Out of a random sample of 272 cases of "dermatitis" admitted to the Chamber of Mines Hospital over a 5-year period, 14·3% of the patients had prickly heat. These were cases of disabling sickness requiring prolonged treatment, and less severe cases are far more numerous. Most of these men with prickly heat came from the Orange Free State and Klerksdorp areas, and are possibly associated with the type of ventilation that prevails in mines in the developing stage. The appearance of prickly heat often coincides with a transfer to a hotter and more humid working place. The authors have seen a number of cases of prickly heat complicating other dermatoses such as contact eczema. A miner may develop prickly heat after he has worked in a stope for some years when there has been no obvious change in the thermal environment.

Miners sometimes develop prickly heat after returning to work from a period of leave, and it is suggested that this may be due to a greater tendency for keratin plugs to form in the sweat pores as a result of thickening of the stratum corneum after exposure to sunlight. Once a miner has developed eczematization or lichenification of the skin lesions he is rarely able to return to work in the environmental conditions which originally caused the prickly heat.

In the discussion of the paper Dr. BARRY contributed information about 88 cases of prickly heat which had occurred at Van Dyk Mine. Most of these occurred in the summer when wet-bulb temperatures in the stopes were about 4°F. higher than in the cool months, and the men doing the hardest work suffered most. *Thomas Bedford*

WYNDHAM, C. H. & COOKE, H. M. **A Review of the Chamber of Mines Acclimatization Procedures.** *Proc. Mine Med. Officers' Ass.* Johannesburg. 1958, May–June, v. 38, No. 364, 10–21. Discussion 21–4.

In gold mines of the Transvaal and the Orange Free State a 2-stage procedure for acclimatizing African recruits to heat was introduced about 5 years ago. The men are set to work at a rate which is roughly the normal rate for the mine, for the first 6 days where the wet-bulb temperature is only moderately high (*e.g.* 86°F.), and for the next 6 days where it may be 91° or 92°F. During the acclimatization period the work is done under European supervisors who have been trained for the task. Mouth temperatures are used to detect abnormalities and to check on labourers who are reported as sick by the African boss boys. A carefully standardized code of practice is applied.

Earlier observations on 229 labourers showed that the average rectal temperature exceeded the oral temperature by 1·2°F. (standard deviation of difference, 0·64°F.), and the coefficient of correlation between the two temperatures was 0·83.

A useful outcome of routine acclimatization under supervision has been the prompt detection of illness in recruits. An analysis is given of the diagnoses of the causes of illness in 126 recruits who were sent to hospital with hyperpyrexia.

Observations have shown significant loss of acclimatization after as little as 6 days away from hot conditions. After such an absence some re-acclimatization is necessary if the incidence of heat stroke is to be kept as low as possible.

The 2-stage method of acclimatization has not been used in all the mines throughout the past 5 years, and cases of heat stroke, some of them fatal, still occur

every year. Figures relating to one mine show a striking fall in the number of cases of heat exhaustion after the introduction of the acclimatization routine.

When hyperpyrexia occurs prompt action to cool the victim is necessary. Trials have been made of various methods of body cooling in the mine. Cooling for 1 hour with the water from a hose pipe at about mine temperature (*e.g.* 87°F.) was the most effective of the methods tried.

Details of the way in which the acclimatization routine is applied are given in the second part of the paper. *Thomas Bedford*

Hygiene of Buildings

HOUSING AND BUILDING CONSTRUCTION

Don, G. G. **Towards a Housing Policy.** *Roy. Soc. Promotion Health J.* 1958, Sept.–Oct., v. 78, No. 5, 634–41.

In this vigorous paper the author looks back at the history of housing in the 19th Century, when Charles Dickens described the Common Lodging Houses Act, 1851, as the best ever passed by an English Parliament. This was followed by other Acts, and by the Royal Commission on the housing of the working classes in 1855, before which Chadwick gave evidence which Don describes as "a damning indictment of nineteenth century housing policy".

Things later looked up, and after 1918 there was a boom in building which was a great advance. But we were building badly and the houses were too often poorly planned and ugly, and housing still lagged behind other public health measures. The author ends by insisting that housing is a local and a social service, that we need many more cottages for old people, and that we still, unfortunately, need a comprehensive housing policy. He suggests one, and readers of this stimulating paper will be inclined to agree with his suggestions. *Charles Wilcocks*

HEAT REGULATION, VENTILATION AND LIGHTING

Stoecker, G. C. **Recognition and Control of Radiant Heat.** *Indust. Med. & Surgery.* Chicago. 1958. Aug., v. 27, No. 8, 396–401, 9 figs.

In industrial situations where there is appreciable radiant heat the author and his colleagues use the temperature indicated by the globe thermometer as an index of the combined effects of radiation and air temperature. Any substantial excess of the globe temperature over the air temperature in a warm situation is an indication that conditions can be mitigated by screening the worker from hot radiating sources. The reader is reminded of the value and convenience of polished aluminium for that purpose, and several examples are given of its effective use. In several instances such shielding reduced the globe temperature (referred to by the author as the "radiant temperature") by 20°F. or more, and in one instance by 40°F., *i.e.* from 130° to 90°F.

The author wisely points out that screens used for protection against radiant heat must be maintained clean and bright, for whereas polished aluminium reflects about 90% of the incident long-wavelength radiation a dirty surface may reflect only 20%. *Thomas Bedford*

Sanitation

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

Schinzel, A., with the assistance of Gertraud Augste & F. Locker. Kalkgebirgsquellenstudien (Limnologie). Die Bedeutung limnologischer Untersuchungen. [**The Importance of Limnological (Hydrobiological) Investigations in the Study of Waters from Limestone Formations**] *Arch. f. Hyg. u. Bakt.* 1958, Oct., v. 142, No. 7, 540–58, 7 figs. [30 refs.]

This is a long paper in which there is a description and discussion of the study of waters derived from different types of limestone formation and of the extent to which springs or other water sources at a distance from mountain limestone areas may be associated with or contain ingredients from the limestone area. During the last 20 years the author has studied the thermal, physical, chemical, bacteriological and other biological variations which may occur in water as the result of various factors including that of pollution. This paper is based particularly on experiences of the Vienna water supply, which is described with geographical and geological details. A question which was particularly considered was whether certain springs which form part of Vienna's water supply were

being polluted by surface waters which included a particular river. The methods adopted to attempt an answer to this question are described, but the main emphasis is placed on the hydrobiological study. In a detailed table the biological forms found in the water of the river Salza are compared with those discovered in 2 spring waters. The list contains many items including algae of various kinds, diatoms, amoebae, flagellates, fungal spores, pollen grains, fragments of wood and moss, insect larvae, faecal remains, chitin and small worms. These findings are discussed at length. It is considered that the limnological (hydrobiological) examination of water is a valuable addition to the common methods for water examination. "The most important fact is to find forms or biozoonoses belonging to a characteristic biotop of surface waters." An example of this is given, for *Hydrurus foetidus*, which is normally found only in surface waters, was also found in 1 of the spring waters, thus indicating a pollution of the latter by surface water.

M. E. Delafield

MIDDLETON, F. M. & ROSEN, A. A. **Organic Contaminants affecting the Quality of Water.** *Pub. Health Rep.* Wash. 1956, Nov., v. 71, No. 11, 1125–33, 3 figs. [23 refs.]

The paper describes methods for isolating and identifying the organic materials polluting the sources of water supplies. Results of experiments carried out at the Robert A. Taft Sanitary Engineering Centre, Cincinnati, have been outlined. 3 figures and 23 references are given.

Industrial wastes and domestic sewage are the factors to be considered in the complex of organic pollution. The organic contaminants affecting the quality of drinking water produce taste and odour which are likely to cause complaints by consumers. The organic chemicals occurring in water in concentration as small as a few parts per thousand million may produce significant taste and odour. Apart from the nuisance point of view, the physiological effects may result from high concentrations of these materials in public water supplies.

At the Taft Laboratory a carbon filter has been developed which adsorbs most organic material from water. The carbon is then dried and the organic material is extracted with chloroform or other organic solvent such as alcohol in a Soxhlet extraction. After extraction the solvent is removed by distillation and the residue is subjected to further analysis. Chloroform was used in most studies and has been found to recover those substances responsible for objectionable taste and odour in water. The residual materials are separated into the groups: water soluble substances, acids, bases, neutrals and phenolic materials. The neutral materials are generally the most abundant group, and they can be expected to resist biological and chemical attack. In many instances they appear in treated water. Neutral compounds which may occur in water are aliphatic and aromatic hydrocarbons and their halogen derivatives.

Aliphatic and aromatic hydrocarbons have been isolated from drinking waters obtained from sources in the vicinity of petroleum-refinery waste outfalls. Phenolic materials which are associated with wastes from dyeworks, gasworks and oil refineries impart tastes and odours to water even in concentrations as small as 1 part per thousand million. Such wastes, when reacting with chlorine, produce chlorophenols which have a much stronger taste and odour than phenol itself. Petrochemical wastes have also presented problems recently. Included in this group are alcohols, benzene, ammonia and sulphur. On one occasion, under winter conditions, the taste and odour were reported to have travelled 1,000 miles, and the waste materials responsible were recovered and partially identified from drinking water 400 miles from the point of discharge.

Concentrations of DDT in the range of 1–5 parts per thousand million were found in the drinking water of several cities using rivers for supply. Concentrations below 1 part per million of chlorinated insecticides are toxic to fish.

Synthetic detergents are resistant to biological forces of purification in the stream and will survive the usual water-treatment processes. They are adsorbed by active carbon and small concentrations have been isolated from tap water.

Products of natural origin in water are frequently responsible for taste and odour difficulties. The growth and decay of microscopic organisms such as algae, protozoa and fungi impart objectionable taste and odour to water. Waters from various surface sources have contained substantial quantities of carbonyl compounds which may result from natural decay, oxidation, and life and death processes of plants and other aquatic life.

I. Vahidi

TAYLOR, E. W. **Examination of Waters and Water Supplies.**

[This book was reviewed on p. 182.]

SELENKA, F. Über die Ursachen des Versagens von TTC-Nährböden in der Wasserbakteriologie nebst Vorschlägen zu ihrer Beseitigung. [**Concerning the Causes of Failure of TTC-Medium in the Bacteriological Examination of Water together with Proposals for their Elimination**] *Arch. f. Hyg. u. Bakt.* 1958, June, v. 142, No. 4, 241–60, 5 figs. [22 refs.]

Bacterial counts on water samples obtained with various nutrient agar media containing TTC differed from those obtained on Endo agar used as reference by 0–100%. It was found that the counts on TTC agar were dependent upon the composition and the preparation of the agar medium, and it was concluded that ordinary nutrient agar is therefore not applicable as a basis for TTC agar in the bacteriological analysis of water.

The trouble is due to the absence of ions which activate dehydrogenase which is precipitated in increased quantities as sparingly soluble phosphate compounds by the addition of phosphate or by making the medium strongly alkaline before sterilizing it.

Acidification or the addition of calcium ions in the form of calcium chloride ($CaCl_2$) avoids this trouble.

A satisfactory medium can be produced if the following precautions are taken: the omission of phosphate, slight acidification before sterilization, standardization of the *p*H to 6·1 shortly before pouring the plates, and the addition of 0·2% of a sterile solution of calcium chloride added simultaneously with the tetrazolium salt.

The preparation of a solid nutrient medium containing TTC for the differentiation between old and recent faecal contamination is possible. *E. Windle Taylor*

ZIEMINSKA, S. Porównawcze badania nad obecnością bakterii grupy *coli* i bakteriofagów niektórych chorobotwórczych bakterii jelitowych w wodzie rzecznej. [**Comparative Studies on the Presence of Bacteria of the *E. coli* Group and Bacteriophages of some Pathogenic Intestinal Bacteria in River Water**] *Roczniki Państwowego Zakładu Hig.* Warsaw. 1958, v. 9, No. 3, 225–34, 3 figs. [19 refs.] English summary.

Determinations have been made of the *Escherichia coli* titre and the titre of *Salmonella typhi* Vi, *Shigella flexneri* and *Salm. paratyphi B* phages in 95 samples of water taken over the course of 1 year from the River Vistula between Warsaw and Płock. The phage titrations were carried out on samples treated with thymol for 48 hours at 4°C. in order to kill bacteria, and subsequently enriched by incubation for 24 hours in the presence of the appropriate host bacteria. 273 cultures of the phage were thus obtained, but were found to be mixtures of strains requiring further passages for their separation. A striking feature of the results was the frequency with which phage was detected in the smallest volume of water (0·001 cc.) among the range examined. No correlation could be observed between the *E. coli* titre and the titre of any of the phages isolated, and it is concluded that determination of the phage titre is not a suitable procedure for the routine examination of water. *D. J. Bauer*

See also p. 272, IWAMURA, **Studies on the *coli-aerogenes* Group (10). Effects of Environmental Factors on the Nature of *Escherichia coli*. I. Alteration of the Formic Hydrogenlyase Activity of *Escherichia coli* in the Case of the Environmental Change from Feces to Water.**

METZLER, D. F., CULP, R. L., STOLTENBERG, H. A., WOODWARD, R. L., WALTON, G., CHANG, S. L., CLARKE, N. A., PALMER, C. M. & MIDDLETON, F. M. **Emergency Use of Reclaimed Water for Potable Supply at Chanute, Kan.** *J. Amer. Water Works Ass.* 1958, Aug., v. 50, No. 8, 1021–57, 13 figs. [15 refs.]

The city of Chanute in Kansas suffered a most severe drought in 1956–57 and emergency measures had to be set up to supply water in the form of recirculated treated sewage effluent through a stabilization pond into the water treatment plant, then into the water distribution system and back through the sewage works into the stabilization pond. The complete cycle covered a period of only 20 days.

As well as the usual sewage treatment and water treatment processes, special safeguards included the chlorination of the sewage plant effluent and prechlorination of the water at the waterworks intake.

There were no special problems in the operation of the sewage treatment plant, and the 17 days' retention in the stabilization pond brought about substantial reductions in the biochemical oxygen demand figure and the ammonia nitrogen and detergent contents.

Difficulties, however, were encountered at the water treatment plant and included:—

1. Owing to the high chlorine demand of the raw water it was impossible to obtain a residual of free chlorine for taste and odour control.
2. False high readings were obtained for the residual chlorine figure.
3. There was foaming at the recarbonation basin and in the rapid sand filters during backwashing.
4. There was less effective coagulation and settling with consequent blocking and coating of the filter bed sand.

The treated water had a pale yellow colour and an unpleasant, musty taste and odour. It foamed when agitated and contained undesirable quantities of dissolved minerals and organic substances [abstracter's italics].

Although there were a considerable number of coliform organisms in the raw water during the period of circulation, treatment was sufficient to bring the bacteriological quality up to the level satisfying the United States Drinking Water Standards throughout the period of re-use.

Algae in the raw water varied from 2,000 to 45,000 per millilitre and the predominant organism was *Ankistrodesmus* which was poorly removed by water treatment.

The concentration of amoebic cysts and other parasitic protozoa in the sewage was low during this period and these organisms were not found in the treated water, but cysts of saprophytic protozoa were found regularly in the treated water, indicating the poor efficiency of the treatment plant in removing these organisms.

Virus of the poliomyelitis, ECHO and Coxsackie groups was isolated from treated sewage samples on 2 occasions but no virus was detected in the treated water.

There were no known adverse effects on the health of the consumers from the use of recirculated water, but consumer acceptance of the water was poor and many persons obtained their drinking water from other sources.

It was concluded that the "reuse of sewage treatment plant effluent to supplement deficient water supplies should not be considered or permitted except under the most severe emergency conditions. It is certainly a last resort, to be used only after all other possible sources of supply have been fully investigated".

The authors state that it is doubtful whether the

process could have been continued for more than a few weeks beyond the 5-month period.

E. Windle Taylor

See also p. 295, KELLY & SANDERSON, **The Effect of Chlorine in Water on Enteric Viruses.**

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

MACK, W. N., MALLMANN, W. L., BLOOM, H. H. & KRUEGER, B. J. **Isolation of Enteric Viruses and Salmonellae from Sewage. I. Comparison of Coliform and Enterococci Incidence to the Isolation of Viruses.** *Sewage & Indust. Wastes.* Wash. 1958, Aug., v. 30, No. 8, 957–62, 1 fig.

The intention of this work was to see whether there was a parallel population of coliform organisms or enterococci to viruses in sewage so that the routine bacteriological examination of sewage would give evidence of the virus concentration. The information presented compares the incidence of coliform and enterococci to the occurrence of virus in sewage, with information on the best methods of specimen collection.

During a period of 2 years 1,403 tests were made for the presence of enteric viruses in the sewage of 2 cities. With suckling mice and monkey kidney tissue cultures, viruses were isolated on 118 occasions (8%). The coliform and enterococci counts for a 12-month period followed the same pattern as the concentration of the viruses.

Types I and III, poliomyelitis, Coxsackie and ECHO viruses were isolated from the sewage, and tests on the non-chlorinated final effluent from the residential area sewage plant showed that the virus was not entirely removed by the sewage treatment.

E. Windle Taylor

OLDHAM, L. W. **Investigations into the Effects of a Non-Ionic Synthetic on Biological Percolating Filters.** *J. & Proc. Inst. Sewage Purification.* 1958, Pt. 2, 136–46, 6 figs. Discussion 146–47.

Mr. L. W. Oldham of the Dyestuffs Division of Imperial Chemical Industries has carried out full-scale tests of the effects of Lissapol N, a non-ionic detergent, on biological filters at the works of Macclesfield Corporation, and results of the tests are given in this paper.

2 pairs of filters were used for the test, 1 of each pair being dosed with Lissapol N and the other being kept as control. Each filter in a pair received about the same quantity of settled sewage of approximately the same strength as measured by BOD and permanganate value. The dosed filters were acclimatized by increasing the dose to the experimental figure by monthly steps of 5 p.p.m. The experimental doses used were 50 and 100 p.p.m. (13¼ and 26½ p.p.m. active agent respectively).

In addition, tests were made with various batches of Lissapol N at a total concentration of 300 p.p.m. to determine whether this agent had any toxic or inhibitory effect on the organisms used in the BOD test. No such effects were shown.

Experiments were also made to see if bacteria could be adapted to the conditions on biological filters and be capable of breaking down Lissapol N. Here again no success was achieved and it seems very clear from Oldham's work that this detergent is biochemically inert in the presence of sewage-purification organisms.

During the 3 years of the experiments some of the other filters in the works were taken out of commission with the result that the experimental filters were at times overloaded, both as to organic load and as to hydraulic load. The 100-p.p.m. filter pair received this excessive load during very wintry weather and this experiment was accordingly abandoned after the test filter had been dosed at 100 p.p.m. for about 3 months.

Oldham's conclusions may be summarized as follows:

50 p.p.m. Lissapol N—During acclimatization and for 2 years at full dose 50 p.p.m. of the detergent in settled sewage (BOD 118–281 p.p.m.; permanganate value 31·5–69·1 p.p.m. including the Lissapol N [these figures do not appear in the printed version]) had no appreciable effect on the percentage reduction in BOD and in permanganate value by the dosed filter, although, probably owing to the chemical oxygen demand of the Lissapol N itself, there was a slight increase in the permanganate value of the dosed effluent over that of the control. During acclimatization there was no appreciable effect on nitrification, but at times of overload (hydraulic and organic) nitrification on the dosed filter was inferior to that on the control. It did not appear that this loss of nitrification was permanent.

100 p.p.m. Lissapol N—During acclimatization and for the short period of the test at full dose there was no appreciable difference between the performances of the dosed (feed BOD 108–294 p.p.m.; permanganate value 29·1–81·8 p.p.m. [figures not in the printed version]) and control filters. The permanganate value of the effluent from the dosed filter was, once again, slightly higher than that from the control. At times of excessive overload and bad weather the detergent dose (100 p.p.m.) appeared to increase the rate of deterioration and seriously reduced nitrification.

As has been intimated above, the sewage organisms had no biochemical effect on the detergent, but it was shown that about one-third of the agent was adsorbed in the filter, being discharged with the humus solids. Thus two-thirds of this non-ionic detergent reached the stream to which the effluent was discharged. There was little agitation of the effluent so that there was no trouble from foaming on the works. However, if the effluents were artificially agitated there was more—and more persistent—foam from the dosed filter than from the control. On occasions banks of foam have occurred in the River Bollin; analyses demonstrated the presence of large amounts of anionic detergents.

[Certain figures have been included in this abstract which, though quoted in the original draft of the paper, are not included in the final version as printed.]

Peter C. G. Isaac

RODENT INFESTATION

MINISTRY OF AGRICULTURE, FISHERIES & FOOD. **Biological Methods for the Evaluation of Rodenticides** [BENTLEY, E. W.]. *Technical Bull.* No. 8. pp. iv + 35, 4 pls. [43 refs.] 1958. London: H.M. Stationery Office. [3s.]

The final decision as to the efficiency of new rodenticides and new formulations of existing poisons rests with the government in countries that operate official approval schemes but in Britain this onus rests primarily on the manufacturers. The Ministry of Agriculture, Fisheries and Food, however, also carries out research on rodent control and issues recommendations. This Technical Bulletin No. 8 is addressed in the first place to manufacturers although it will have much interest and value for all who are concerned with the control of rats and mice by poisoning. "One purpose of this bulletin is to discuss the characteristics required of the main types of rodenticides and to describe some of the methods which have been evolved for their investigation" and "The second purpose is to show the difficulties that must be overcome in drawing up specifications for rodenticides and in attempting to standardize tests of their biological effectiveness".

In the introduction there is a classification of present day rodenticides and it is pointed out that only poisons employed against 3 species of rodents are considered in this Bulletin: (1) the common or Norway rat, *Rattus norvegicus*, (2) the ship or roof rat, *Rattus rattus* and (3) the house-mouse, *Mus musculus*.

The subject-matter is clearly presented in the light of modern knowledge and opinion with due reference to the literature which is set out in an appendix. Most of the space is devoted to acute poisons under the headings of determination of toxicity, investigation of palatability, time of onset of poison symptoms, poisons and shyness, field trials and additives. The assessment of chronic poisons is then considered but only in so far as this differs in technique from that of acute poisons. There is also a description of the evaluation of poisonous dusts which though claimed to have advantages over poison-baits have also certain definite disadvantages.

This technical bulletin should be of much value in setting out critically modern viewpoints and methods and so helping to bring about improvements in rodent control for "Unfortunately, in spite of a popular belief to the contrary, the scientific evaluation of rodenticides is far from easy and, from time to time, products appear on the market with little experimental evidence to justify the claims made for them".

M. E. Delafield

Port, Ship and Aviation Hygiene

EJSMONT, W. **The Cases of Illnesses of Deepsea Fishermen on Fishing Waters in 1955.** *Bull. Inst. Marine Med. Gdańsk.* 1958, v. 9, Nos. 3/4, 181–9. [21 refs.]

This is a report from the Institute of Marine Medicine in Gdańsk on the incidence of sickness and accidents among Polish deep-sea fishermen in April to December, 1955. The conditions of work and climatic conditions in the fishery industry are described. Base vessels of 4,000–8,000 tons which supply a flotilla of 100–130 smaller fishing vessels have an ambulance station with a staff composed of a doctor, a dentist, a male nurse and a hospital steward. There is a doctor's room, a room for dental work, X-ray accommodation and a room for physio-therapy. Patients are seen either on the base vessel or medical advice may be transmitted to the fishing vessels by radio. The sickness and accident incidence is described and set out in tables by nature of the condition and by "professional group" *i.e.* deck staff, engine room staff and base vessels staff. Medical advice was given in over 4,000 cases. In the aggregate, injuries occurred in 22% and of disease conditions those of the skin represented 21% of the total. Next in numerical importance were diseases of the joints and muscles (14%), nervous system ("neurosis of the heart and acute headaches" 13%), alimentary system (13%) and respiratory system (12%).

M. E. Delafield

Infestation and Disinfestation

GEORGE, W. M. **Norwegian Scabies.** *Arch. Dermat.* 1958, Sept., v. 78, No. 3, 320–24, 4 figs.

Severe hyperkeratinization distinguishes Norwegian scabies from typical scabies. Thick crusted lesions composed of dried serum and keratin are riddled with burrows containing innumerable parasites and ova. Plaques may occur in multiple areas particularly sites of skin stretching and pressure.

Mongols and mentally defective persons are particularly

liable to be affected. The decrease in plasma vitamin A levels may be a contributing factor in the development of hyperkeratinization in this condition.

Norwegian scabies may be misdiagnosed as psoriasis, keratoderma blennorrhagica or other hyperkeratotic conditions.

Of 2 patients described in this paper 1 had been treated for psoriasis for 6 years while the other was thought to have malignant lymphoma. Patients with Norwegian scabies can infect other persons with typical scabies and frequently do so. *H. T. H. Wilson*

Food and Nutrition

FOODSTUFFS

(Composition and Bacteriological Control)

NICKERSON, J. T. R., PROCTOR, B. E. & GOLDBLITH, S. A. **Freezing and Irradiation.** *Amer. J. Pub. Health.* 1958, Aug., v. 48, No. 8, 1041–8, 1 fig.

The authors give a general assessment of possible health risks from foods frozen in their raw condition, those frozen after preliminary preparation and a much newer type of pre-cooked frozen food. The use of the last group is being widely extended. The authors do not consider that the point which has been raised, namely that the pre-cooking makes the foods more vulnerable to bacterial invasion, is of importance in practice. Sanitary care is emphasized for all frozen foods but not especially for pre-cooked foods. However, it is suggested that the time has arrived for setting up sanitary standards for frozen food and that these are especially necessary for the pre-cooked frozen food products.

The problems of bacterial growth after defrosting are briefly considered, and the authors consider that the risks of household mishandling are not high, as shown by practical experience.

The last part of the paper deals with food irradiation in relation to public health. Irradiation which is practical will not destroy *Clostridium botulinum* spores. Total sterilization of food products by treatment with cathode or gamma rays at levels as high as $4{\cdot}8 \times 10^6$ rep appears at the present time to have possibilities only with certain meat, fish and poultry products. One difficulty is the production of unsatisfactory products causing oxidation changes, browning and other undesirable results. The irradiation treatment of whole eggs and egg-yolk products to destroy Salmonella organisms has not as yet given satisfactory results. Undesirable after-results are particularly liable to occur with milk, mainly off-flavours, and these are discussed.

[The paper is useful as a general and authoritative statement of the present position in this field of food preservation.] *W. G. Savage*

KEMPE, L. L., GRAIKOSKI, J. T. & BONVENTRE, P. F. **Combined Irradiation-Heat Processing of Canned Foods. II. Raw Ground Beef inoculated with Spores of *Clostridium botulinum*.** *Applied Microbiol.* Baltimore. 1958, July, v. 6, No. 4, 261–3, 1 fig. [10 refs.]

The vehicle used was raw ground beef from which dissolved metabolic gases were removed by evacuation under vacuum (repeated 3 times). The beef was then packed into No. 1 picnic tin cans which were subjected to degassing under vacuum. The meat was inoculated with 1 ml. of a spore suspension of *Cl. botulinum* 213B estimated to contain 5,000,000 spores per can. The cans were subjected to a double process, *i.e.* irradiation with an F_0 of 0·2 after irradiation with 1·3 megarep of gamma rays from ^{60}cobalt and ordinary heat sterilization. [F_0 = the number of minutes required to sterilize the can of meat at 250°F. when the Z value (the slope of the thermal death-time curve) equals 18.] Adequate control tins were used. The results are shown in a chart. The conclusion reached was that, under the conditions of the experiments, raw ground beef was sterilized by 1,400 megarep pre-irradiation plus an F_0 between 0·13 and 0·28. The experiments indicate that the pre-irradiation treatment is as effective in raw meat as it had previously been with cooked meat [this *Bulletin*, 1958, v. 33, 969].

W. G. Savage

MILLER, W. C., Jr. **Developing an Ordinance and Code for Food Vending Machines.** *Pub. Health Rep.* Wash. 1958, Oct., v. 73, No. 10, 903–9.

"The history of automatic merchandising starts about 200 B.C.; the first vending machine of record dispensed holy water in a Greek temple in Alexandria, Egypt." Vending machines first appeared in the United States in the late 1880's since when their use has expanded to such an extent that "A billion dollars for foods and beverages was dropped into coin slots in 1957". These machines have been developed to dispense perishable products such as hot and cold sandwiches, meat dishes, soups and salads. There are even some "prototype machines which hold precooked frozen meals and dispense these meals hot in a matter of seconds". Many States and communities and the trade organization of the industry requested the Public Health Service to develop a model sanitation ordinance and code for vending machines. After 4 years of study and investigation the U.S. Public Health Service issued "The vending of foods and beverages; a sanitation ordinance and code; 1957 recommendations of the Public Health Service. PHS Pub. No. 546. Washington, D.C., U.S. Government Printing Office, 1957". This publication represents the views of State and local officials and the vending machine industry.

In this article there is an account of the history and growth of vending machines and a description and discussion of the difficulties and points which were considered in drawing up the model ordinance. Details are given under the headings of permit requirements, sanitation requirements and other requirements such as the location of the machine, its construction and maintenance, the water supply, disposal of waste from the machine and protection from contamination. A number of States are now using the recommended ordinance and code or some of its provisions as a basis for State laws and regulations.

M. E. Delafield

HOPPER, S. H. & ADAMS, H. S. **Copper Poisoning from Vending Machines.** *Pub. Health Rep.* Wash. 1958, Oct., v. 73, No. 10, 910–14.

This paper contains a description of some investigations which were undertaken to determine the amounts of copper which might appear in carbonated drinks provided by certain vending machines. A number of cases of acute gastric upset "that appear to be copper poisoning" had been reported in persons who had consumed drinks from these machines. These post-mix machines release 1 oz. of flavoured syrup into a cup and then add 5 oz. or more of carbonated water. Some cases of alleged copper poisoning are described and the toxicity of copper is discussed with reference to the published opinions on this matter which are by no means unanimous. Some experiments on the amounts of copper found in the water contained in a copper tube after different periods of exposure to carbon dioxide under pressure or at varying hydrogen ion concentration are described. In the conclusion it is stated that "If the check valves in a post-mix type vending machine do not function correctly, carbon dioxide may enter the water supply line". If this water line is made of copper the CO_2 or carbonated water will react with the copper and under certain conditions the copper going into solution could be quite large. Copper poisoning could then occur and although this poisoning has occurred in only very few persons, it could be prevented by attention to certain technical points in the construction of the machines.

M. E. Delafield

CECIL, J. T. **Milk and the Housewife. A Small Survey into the Storage of Milk, the handling of Milk by the Housewife and her Knowledge on the Subject of Milk.** *J. Roy. Inst. Pub. Health & Hyg.* 1958, Oct., v. 21, No. 10, 267–77, 1 fig.

In this paper there is some historical account of milk legislation since the Milk and Dairies Consolidation Act, 1915, which became operative in 1922. At the present time safe, clean and palatable milk is delivered to households, and the survey here described was made to discover how housewives handled and stored the milk in the home. The survey was conducted in the village of Leigh in Kent which has a population of 1,516 in 427 private households. A sample of 70 housewives were interviewed to obtain the required information and also to test the housewives' knowledge of milk by a questionnaire. The findings of the survey are described at considerable length with 8 tables which set out the differences in these findings in the 5 social classes. The main conclusion is that "the housewife seems to treat her milk in a reasonably hygienic and efficient manner" yet "her knowledge on the simple facts of milk could well be improved" by various methods which are suggested.

[The method of sampling of the 70 housewives used is not stated. Percentages are calculated even for very small numbers.] *M. E. Delafield*

FRANKLIN, J. G., WILLIAMS, D. J., CHAPMAN, Helen R. & CLEGG, L. F. L. **Methods of assessing the Sporicidal Efficiency of an Ultra-High-Temperature Milk Sterilizing Plant. II. Experiments with Suspensions of Spores in Milk.** *J. Applied Bact.* 1958, June, v. 21, No. 1, 47–50.

The plant tested was an APV HX-type heat exchanger installed in a dairy. Spore suspensions of *Bacillus subtilis* from milk were used and added to raw milk to give a final concentration of 5×10^6/ml. Treatment temperatures of 130·5°, 132·0°, 133·5°, and 135·0°C. were tested with the tube set at the minimum holding period. Under adequate precautions samples were collected. The results of the plant experiment are set out in a table and show that a 99·99999% destruction of spores was achieved at about 130·5°. This is a temperature lower than is required to give a similar destruction in water [this *Bulletin*, 1957, v. 32, 1178] and suggests an inhibitory effect exerted by the milk.

W. G. Savage

FRANKLIN, J. G., WILLIAMS, D. J. & CLEGG, L. F. L. **Methods of assessing the Sporicidal Efficiency of an Ultra-High-Temperature Milk Sterilizing Plant. III. Laboratory Determinations of the Heat Resistance of Spores of *Bacillus subtilis* in Water and in Milk.** *J. Applied. Bact.* 1958, June, v. 21, No. 1, 51–7, 5 figs. [10 refs.]

This paper, the third in a series [see above], is a laboratory report on the heat resistance of *B. subtilis* spores in water and in milk from several sources. The figures and charts show that the numbers of survivors were lower in milk than in water. The types of milk used were ultra-high-temperature (UHT) sterilized milk, autoclaved whole homogenized milk and autoclaved skim milk. The differences may be due to several causes, but the one suggested is the presence of some inhibitory agent in the milks. There appear to be 2 inhibitory effects in UHT milk, one associated with the heating medium and the other with the recovery medium used in the dilution counts. These are being further investigated. The authors consider that, provided the thermal characteristics of the spores concerned are known, it seems possible to predict by theoretical methods how spores will behave in a UHT milk sterilizing plant without resort to bacteriological experiments with the plant itself. *W. G. Savage*

THOMAS, S. B., HOBSON, Phyllis M. & ELSON, K. *Coli-aerogenes* **Bacteria from Farm Dairy Equipment and Raw Milk.** *J. Applied Bact.* 1958, June, v. 21, No. 1, 58–64.

The samples were collected from rinses of dairy equipment and from both morning and evening milk. The dilutions were added to MacConkey's broth and incubated for 5 days at 30°C. This temperature was found much more satisfactory than 37°C. After discarding duplicates there were left 429 cultures from dairy equipment and 611 from raw milk. These findings are summarized in a table which also sets out the varieties within each group. The *coli-aerogenes* strains are classified under 7 groups, *i.e. Escherichia coli* I, *E. coli* II, *Citrobacter freundii* I, *C. freundii* II, *Klebsiella aerogenes* I, *K. cloacae* and *K. aerogenes* II.

There were no marked seasonal differences in the different species, although *E. coli* formed a slightly higher proportion in winter, nor were there any marked differences between dairy equipment and the milk. *Klebsiella* constituted the dominant genus with *K. cloacae* the most common species. *C. freundii* was relatively abundant, forming 20% of the equipment group and 30% from milk. The incidence of *E. coli* was relatively low. *W. G. Savage*

EGDELL, J. W., LOMAX, Kathleen L., ADAMS, R. P. & AITKEN, Margaret J. **Bacteriological Studies of Immersion Cleaning of Milking Equipment on Commercial Farms.** *J. Applied Bact.* 1958, June, v. 21, No. 1, 109–17.

The immersion cleaning process with caustic soda or chlorine is well-known and is not described in detail in the paper. A survey of its effectiveness was applied to selected commercial farms and the samples included rinse and swab samples from the milk vessels and similar samples from milking machine clusters and lids and gaskets of vessels. One table shows that of 9 farms frequently sampled only 1 was repeatedly unsatisfactory. As regards the milking vessels, out of 413 samples only 8% were really unsatisfactory. The gasket and lid samples were mainly fairly good but the percentage unsatisfactory was 18% for the cluster samples.

A detailed study is included at the unsatisfactory farm to try to relate the poor findings to particular factors. The poor results were caused partly by sporing bacteria which survived the caustic soda treatment and partly by non-sporing organisms chiefly chromobacteria and micrococci.

Another study of farms deals with the various sources of contamination and their relationship to the bacterial findings. The non-sporing organisms are found in abundance on the surface of dirty wash troughs and under certain conditions re-contamination of the milking equipment can occur during the rinsing operation. A number of suggestions are advanced to reduce these sources of contamination.

W. G. Savage

FOOD POISONING

SAHA, A. L. & GANGULI, N. C. **An Outbreak of Staphylococcal Food Poisoning from Consumption of Dahi.** *Indian J. Pub. Health.* 1957, Jan., v. 1, No. 1, 22–6, 1 map.

This is an account of an outbreak of staphylococcal food poisoning which occurred in Paikpara, Calcutta. The history of the outbreak and its investigation are described with a map and tables of the age distribution of the patients and the severity of their gastro-intestinal symptoms. A total of 67 persons belonging to 26 families were affected and of these 12 were under 5 years of age and 17 were between 5 and 15 years old. All the patients had consumed *dahi* (milk curd) within ½–4½ hours of being taken ill. This *dahi* had been prepared by a particular local confectioner who, when charged by his customers with selling a bad product, became indignant and thereupon himself consumed some of the same lot of *dahi* to prove that it was harmless. Within 2 hours he developed the typical symptoms of gastro-enteritis. The unsold pots of *dahi* could not be examined as they had been destroyed by some "irritated young men". Only a single sample left over in a consumer's house was available and from this coagulase-positive *Staphylococcus aureus* was isolated. No definite information was obtained of the source of the organism. Detailed information could only be collected from 10 families with a total of 130 persons. Of this total 32 persons consumed the *dahi* and 27 were taken ill. The illness was mild in 12 persons but severe in 12 and 1 male child aged 2½ years died.

The literature of staphylococcal food poisoning from other countries is discussed briefly. It is considered to be likely that outbreaks of this poisoning are not rare in India but are not being recorded because the general attention of the Indian workers has not yet been drawn to the subject. *M. E. Delafield*

CLARENBURG, A., KAMPELMACHER, E. H., VAN KEULEN, A. & DE NOOIJ, E. Epidemiologische bevindingen bij een vleesvergiftiging, veroorzaakt door *S. typhi murium.* [**Epidemiological Data on an Outbreak of Meat Poisoning caused by** *Salmonella typhimurium*] *Tijdschr. v. Diergeneesk.* 1958, Dec. 1, v. 83, No. 23, 1217–19.

The English summary appended to the paper is as follows:—

"Several families were found to be infected with *S. typhimurium* following the ingestion of meat products prepared from a privately slaughtered pig. In addition, this *Salmonellae*-type was also found to be present in mice and in a cat. All strains appeared to belong to the fermenting type 10.

"The epidemiology of this case of food-poisoning, which was probably due to an animal which caught the infection while still alive, is subjected to further analysis."

HALSTEAD, B. W. & SCHALL, D. W. **A Report on the Poisonous Fishes of the Line Islands.** *Acta Tropica.* Basle. 1958, v. 15, No. 3, 193–233, 4 figs. [Numerous refs.]

"This is the fifth of a series of epidemiological reports concerning the poisonous fishes of the tropical Pacific." Previous reports by Halstead and his co-workers dealt with the Phoenix Islands, Johnston Island, the Galápagos Islands and with Cocos Island [see, for example, this *Bulletin*, 1954, v. 29, 649]. The present study was supported by the U.S. Public Health Service and the Office of Naval Research with generous assistance from a number of other authorities which are named.

There are 19 scattered islands in the group of Line Islands which lie near the Equator. The islands included in this report are Malden, Christmas, Fanning and Washington which are under British rule and Jarvis, Palmyra and Kingman Reef which are administered by the United States. All these are small low-lying coral atolls and their geography and characters are described in considerable detail. There is an account of the materials and methods used in collection of specimens of fish and of the mouse toxicity tests which were carried out with extracts of fish muscle and other organs. The identification of the fish was made mainly by the authors but helped in some instances by other experts who are named and certain reference works of which a list is given in the text. A total of 747 specimens of fishes belonging to 87 species of over 20 families were tested for toxicity and of these 337 specimens of 58 species were found to yield toxic extracts from 1 or more of the tissues which were examined. Excluded from these figures are specimens of tetraodontoid fishes (the puffers) since they are generally considered to be poisonous wherever they are found. A detailed table of about 19 pages contains particulars of the scientific names of family and species of the tested specimens, their common names, the locality where they were caught and the degree of toxicity, if any, of the fish extracts.

It is of interest that no cases of fish poisoning in the Line Islands were recorded before 1943 but that since that date the incidence has increased and Japanese reports also indicate that there has been a marked increase in poisonings from marine animals since 1945 in the western Pacific. In the discussion there is stress on the importance of the subject of fish toxicity regarded from the view point of the food supply of a world with a rapidly increasing population. *M. E. Delafield*

MASI, A. T., ARMIJO, R. & TIMOTHEE, R. A. **Observations on the Nature of Great Barracuda Food Poisoning encountered in Puerto Rico.** *Bol. Asoc. Med. de Puerto Rico.* 1958, July, v. 50, No. 7, 255–8.

The owner of a food store bought 2 reputedly freshly caught "picua" (great barracuda or *Sphyraena barracuda*), each weighing about 15 lb., from a travelling fish merchant. These fish were kept in a good refrigerator overnight and portions of 1 of them were sold next morning to 2 customers. On the same day the families of both customers consumed fried barracuda. In 1 family 4 of its 5 members were taken ill but a child who had not had fish remained well. Among the 8 members of the other family 6 became ill after eating fish but 2 who had abstained suffered no symptoms. The incubation period ranged from 1 to 6 hours. Those persons who had eaten the largest amounts of fish had the severest symptoms which were abdominal pain, nausea and vomiting, mucoid diarrhoea and painful sensations in the extremities. All the patients made a complete recovery in a period of about 4 hours up to 2 days, although the pain in the extremities persisted for about 4 days in the severe cases. No laboratory analyses of secretions or excretions of the patients could be carried out, but some animal feeding experiments on cats with the uncooked fish indicated that the barracuda which had caused the human poisonings was toxic for cats but that the other fish was harmless. In the discussion there is reference to published reports on barracuda which is at times found to be poisonous [this *Bulletin*, 1954, v. 29, 649; 1957, v. 32, 172]. *M. E. Delafield*

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

ZENT. F. BAKT, I. Abt. Orig. 1958, v. 171, No. 8, 545–615, 14 figs. [Numerous refs.] Vortrag anlasslich des 3. Colloquiums über Fragen der Lysotypie vom 28. Sept. bis 2. Okt. 1957 in Wernigerode/Harz. [**Report on the Third Symposium on Phage Typing**]

H. RISCHE, K. ROHNE, P. NICOLLE and Gisèle DIVERNEAU (p. 546–51) report a study of the constancy of the "subtype" reactions of strains of *Salmonella typhi*, phage type A, after passage through 3 guinea-pigs by the gall-bladder route. The subtype reactions are based on susceptibility to a number of phages, only 2 of which are Vi phages. Of 225 strains isolated from the faeces of the animals, 194 gave routine and subtype

reactions identical with those of the original strains, while 31 were untypable with the routine phages but gave the same subtype reactions as the originals. P. NICOLLE and Gisèle DIVERNEAU (p. 552–9) take the last point further and report that the various Vi types of *Salm. typhi* have characteristic patterns with the 8 complementary phages so that not only can these phages be used to subdivide the main Vi-phage types, but also the 6 non-Vi phages can be used to recognize the probable "Vi type" of Vi-deficient strains. This "identification" can be supplemented by tests with more phages isolated from the subtypes themselves. P. TOMASIC (p. 560–7) had applied Nicolle's method of subdivision of supplementary phages to a number of strains of *Salm. typhi*, phage type A, isolated in separate foci of an epidemic in Yugoslavia. Although the supplementary phages decreased in titre over the 3 years of the investigation, all the strains isolated from any one focus had identical reactions with them. Neither of DESRANLEAU'S subtypes could be recognized.

H. RISCHE, (p. 568–72), using a provisional typing scheme devised by FELIX and BANKER, examined 100 strains of *Salm. paratyphi A* from various countries in Eastern Europe; 67 proved to be type I and 19 were thought to be "type 4 degrading". The types were stable on animal passage.

R. WAHL and J. FOUACE (p. 573–83) describe the changes in phage-typing pattern of staphylococci [utilizing phage filtrates diluted 1 in 10 and therefore much stronger than routine test dilution (RTD)] that result from spontaneous loss of prophage and from artificial lysogenization. The observations can be best explained if it is supposed that 1 prophage is able to block the activity of several different phages. These phages need not all be within the same lytic group [serology is not discussed]. Some of the lysates used in routine typing contain more than one phage, so that various lysogenic variants may be isolated from the mixture of one staphylococcal clone with one filtrate.

Věra MATĚJOVSKÁ and J. JELÍNEK (p. 584–9) report a few experiments showing that reduction in the thickness of the bacterial lawn increases the apparent titre of staphylococcus phages. Staphylococci subjected to passage through antibiotics were found to lose some of their sensitivity to bacteriophages.

B. SCHMIDT and V. LENK (p. 590–600) compared the phage type and antibiotic (especially streptomycin) resistance of 569 strains of *Staphylococcus aureus*. Phage-untypable strains were rarely very resistant; 13% and 16% of Groups I and III strains respectively were streptomycin-susceptible. Differences were also found among strains with different patterns within the groups.

M. CIUCA, N. NESTORESCU, Marcella POPOVICI, Ecaterina ALEXENCO, Stela NOVAC and Aurica CHEPTEA (p. 601–5) recount the great frequency of staphylococci of phage type 80 as a cause of infections and in healthy carriers in maternity hospitals and children's clinics in Rumania. In contrast, in a surgical clinic, staphylococci of Group III were predominant. Drug resistance was commonest among the type-80 strains.

R. PAKULA and W. WALCZAK (p. 606–11) describe the isolation of phage-surviving variants of groups A and C streptococci which had altered cell-wall polysaccharides so that they no longer showed a reaction with their specific grouping sera. It was possible to make specific antisera against the variant polysaccharides. The rhamnose-glucosamine ratio in the variants differed from that of their parents.

J. F. VIEU (p. 612–15) reports the testing of 90 strains of *Proteus hauseri* with 21 phages isolated from sewage. 10 different types accounted for 82% of the strains.

R. E. O. Williams

CARTER, C. H. & LEISE, J. M. **Specific Staining of Various Bacteria with a Single Fluorescent Antiglobulin.** *J. Bacteriology*. 1958, Aug., v. 76, No. 2, 152–4.

Earlier adoptions for bacteriological purposes of the technique of staining viruses in tissue with fluorescent combined antibody introduced by COONS and KAPLAN [this *Bulletin*, 1950, v. 25, 730] have been extended. It is shown that the recognition of bacteria by fluorescent antibody may be more simply effected if the bacteria are first stained by the appropriate antiserum and then the globulin, which has combined with them, is stained with an antiglobulin serum appropriate to the globulin of the animal which has furnished the antibody.

Observations on *Brucella suis*, *Pasteurella pestis*, *Br. tularensis* and *Vibrio cholerae* have been made in this way and it is possible, after trying several different sera with negative result, to wash these off and finally by treating the slide with serum specific for the bacteria in the film, to get a positive result with the fluorescent antiglobulin.

[See also this *Bulletin*, 1955, v. 30, 369.]

J. W. McLeod

KLEIN, F., METCALF, S. N. Jr. & LINCOLN, R. E. **Laboratory Apparatus for Collection of Flocculated Vegetative Bacterial Cells.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 363–8, 5 figs.

A number of hydrophilic colloids, by adsorption of a flocculant on the hydrated surface, can flocculate cells of various bacterial species. Cells collected by flocculation, unlike those collected by centrifugation, can easily be redispersed. A viable cell recovery of 75%, with a 20-fold concentration, can be obtained in 6 hours' settling time. This needs efficient collecting vessels. Various designs of vessels for collecting *Brucella suis*, with 2% gelatin as flocculant, are described, and the effects of vibration and angle of incline of the surface on to which the cells precipitate were tested. It was concluded that in sedimentation columns (cylindrical glass columns with a stainless steel liner) the free fall of the bacterial cell should be kept to a minimum; 45° was the optimal angle, and vibration increased the efficiency of the process. A vibration at the rate of 3,600 cycles per minute with an amplitude of less than 0·008 inch gave flocculated cells of *Br. suis* a sliding velocity of 15·9 inches per hour. Cultures grown in the presence of 2% gelatin flocculate as well as those to which a similar concentration of gelatin was added after incubation.

E. Agius

MANSI, W. **Slide Gel Diffusion Precipitin Test** [*Correspondence.*] *Nature.* 1958, May 3, v. 181, 1289–90, 1 fig.

By this technique a more rapid result can be obtained than by the plate method. The melted medium is spread to a constant depth between 2 grease-pencil lines (or 2 thin zinc oxide tapes) 4 cm. apart on a microscope slide, 1 cc. of medium being used for the purpose. The basins in the medium are cut with a stainless steel tube through a Perspex guide, in 2 hexagonal units of 7 basins, 1 being central. The reagents (antigen and antisera) are placed in the basins by means of a fine pipette, and the slide is incubated at 37°C. in Petri dishes.

An example is illustrated in which the lines of precipitation appeared clearly in 90 minutes; there is an advantage in clarity if the reading is taken as soon as the reaction is expected to appear; later the lines may become blurred. *Charles Wilcocks*

PIJPER, A. **Bacterial Flagella and Motility.** *Ergebn. Mikrobiol. Immunitätsf. u. Exper. Therap.* 1957, v. 30, 37–95, 38 figs. on 4 pls. [344 refs.]

This extensive review of the literature has been written by a scientist who has previously expressed a definite point of view on the nature of bacterial flagella. In the present paper he discusses the subject under headings dealing with methods of investigation, the nature of various types of flagella, bacterial motility and related subjects. There is no general summary and the paper should be read in full.
Charles Wilcocks

PEASE, P. **Electron Microscopy of the Processes of Regeneration of Bacillary Forms from Filterable and Non-Filterable Stages in the L-Form of Bacteria.** *Giorn. di Microbiol.* Naples. 1958, Jan.–Feb., v. 5, No. 1, 35–8, 13 figs. on 3 pls.

The English summary appended to the paper is as follows:—

"The generation of the bacillary form from 'large bodies' (protoplasts) and 'small bodies' (filterable granules) of bacterial L-forms is compared. Both are capable of multiplication. The former may revert directly to bacilli, the latter only after aggregation into larger granules and filaments."

FLOOD, C. M. **An Injection Unit used instead of the Hypodermic Syringe.** *Lancet.* 1958, Nov. 22, 1114–16, 1 fig.

This article is a description and commendation of a sterile disposal injection unit which has been commercially available for some years under the name of Ampin. Each unit consists of an ampoule containing the injection fluid and an inert gas under pressure. A sterile needle protected by a glass guard is connected by a flexible tube to the ampoule neck. A gauze filter is provided at the base of the needle. In use the needle guard is removed by breaking at a scored mark and the needle inserted into the patient. If the needle is in a vein the tube can be squeezed and released to aspirate blood, which will stain the filter. With the ampoule held so that the gas is above the fluid its neck is broken and the gas injects the fluid.

The advantages claimed are accuracy of dosage, guaranteed sterility with freedom from homologous serum jaundice, a new sharp needle for each injection, prevention of contact allergy in nurses and a saving of time and suitability for home injection by the patient or his relatives. The Ampin is also less liable to be pilfered by addicts. The possibility of air embolism is considered remote—even if the device was used upside down the maximum amount of gas that could be injected is 4 ml. and larger quantities have been inadvertently injected without ill effect.

Ampins are available filled with a variety of fluids and at a cost (exclusive of drug) of 7½d.–8d. each according to the size of the needle. It is hoped that increased demand will reduce the cost considerably. (The current price for a sterile syringe service is about 5d. per unit.)

The author reports a trial of Ampins in a maternity hospital. After initial reluctance the response of the nursing staff was enthusiastic. 95% of 900 injections so given were satisfactory but only 88% of 80 intravenous injections; this is attributed to the fact that the former were given by nurses who had practised on dummy units filled with water and the latter were given by doctors without such practice. The author concludes that the Ampins are more economical than conventional sterile syringes and should be considered as an alternative to a central syringe service.

[Ampins are obtainable from Ampin's Ltd., Guildford.] *J. C. Kelsey*

THOMAS, C. G. A., LIDDELL, J. & CARMICHAEL, D. S. **Cleansing of Hospital Blankets.** *Brit. Med. J.* 1958, Nov. 29, 1336–8.

The efficiency of a laundering process was tested by taking sweep plates from blankets before and after washing. The process was one in which a mixture of sodium sesquicarbonate and an anionic detergent based on sulphonated fatty alcohols was used at 37·8°C. After 2 rinses the blankets were dried by air at 82°C. A medium containing phenolphthalein diphosphate was used for the sweep plates so that *Staphylococcus aureus* could readily be detected. 2 plates were taken from each blanket. 100 blankets straight from wards yielded a total of 47,818 colonies of which 1,085 were *Staph. aureus*. Washed blankets yielded 2,034 and 22 colonies respectively. Thus washing greatly reduced the total count. Initially 87% of blankets yielded *Staph. aureus*, but after washing 15% were still positive. This finding is the more significant because the antibiotic sensitivities of the staphylococci were similar to those isolated concurrently from patients in the hospital.

Studies with settle plates and aerosols of *Serratia marcescens* [*Chromobacterium prodigiosum*] were largely negative in that no aerial recontamination of washed blankets could be demonstrated; the air of the room where dirty blankets were sorted was, however, shown to be heavily contaminated.

The authors conclude that the process described, though not ideal, is better than many in use elsewhere, but agree with FRISBY [this *Bulletin*, 1958, v. 33, 63] and others that blankets made of boilable material may be the ultimate solution to this very urgent problem..

[BLOWERS and WALLACE (*ibid.*, 1955, v. 30, 897) described a very effective laundry process, with cetyl trimethylamine bromide at 37°C., which probably yields better results than the one described here. If a working temperature of 60°C. can be accepted, vegetative organisms can be virtually eliminated (*ibid.*, 1958, v. 33, 1167 *bis*).] *J. C. Kelsey*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order:—General; Antibiotics; Other Therapeutic Substances; Disinfection.

MORENZ, J. Über die routinemässige Verwendbarkeit der Papierblättchenmethode zur Resistenzbestimmung. [**On the Applicability of the Paper Strip Method for the Routine Measurement of Resistance**] *Ztschr. f. d. g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Jan.–Feb.–Mar.–Apr., v. 4, Nos. 1/2, 21–32, 7 figs.

Filter paper strips are soaked in solutions of 5 antibiotics and 3 sulphonamides and dried. 3 different concentrations are used, intended to correspond to those attainable in the blood by ordinary and by high dosage and thirdly that attainable by local application or in the urine or bile. Solid growth of the organism to be tested is suspended in saline to give 1/5 "Widal opacity" (defined) and this suspension is further diluted to a very varied extent according to species (streptococci not at all, staphylococci 1 in 100, *Proteus* 1 in 5,000); a loopful of this suspension is then streaked across a plate and 3 strips containing the drug are applied at right angles to it. Such cultures are not illustrated and it is not clear how many organisms per plate (if more than one) can be tested. Diffusion of the drug is allowed to proceed for 4 hours before incubation is begun.

The author examines the effect on the results of this test of some of the factors which are well known to affect agar diffusion tests generally (composition of medium, inoculum size, depth of medium etc.) and presents some comparative findings by a tube dilution test showing that the 2 methods usually give concordant results. [The author gives no reason for preferring strips to disks, which occupy much less space.]
L. P. Garrod

DENNIG, H. Über Nebenerscheinungen bei antibiotischer Behandlung. [**Side-Effects of Antibiotic Treatment**] *Deut. med. Woch.* 1958, Oct. 17, v. 83, No. 42, 1849–51, 1882–83.

To determine how serious is the problem of antibiotic reactions, the author obtained data about all those occurring in 1 year in his hospital in Stuttgart (197 beds). The following were the principal antibiotics used, the numbers of patients given them, and the reactions observed: penicillin (170), 5 patients had rashes; streptomycin (50) 1 local reaction only; penicillin + streptomycin (220), 5 rashes and 1 glossitis; tetracycline (117), 1 rash, 1 febrile reaction and 6 cases of diarrhoea including 1 fatal membranous enterocolitis (but also with severe disease elsewhere); chloramphenicol (50), 2 rashes, 2 diarrhoea, 1 *Candida* pneumonia (fatal). The view is taken that these dangers and inconveniences have been exaggerated.
L. P. Garrod

MARTIN, F. J. **Anaphylactoid Reaction to Oral Penicillin: Report of a Case.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 662–65. [10 refs.]

A woman aged 52, who had had much penicillin before and once reacted to an injected dose with urticaria, bought some penicillin tablets (containing 50,000 units each) in a drug store because she had a cold, took 1 and within 30 seconds had a sense of suffocation and collapsed. When seen by the author she was cyanosed and pulseless. She recovered after treatment with Levarterenol [noradrenaline], Neopavrine, Solucortef, Coramine and Nalline. The prevention of such episodes is discussed, the conclusion being reached that the best preventive is to use penicillin "only when absolutely indicated". *L. P. Garrod*

MIYAMURA, S. **Bactericidal Action of Chloramphenicol on *Escherichia coli*.** *J. Bacteriology.* 1958, June, v. 75, No. 6, 617–22, 5 figs.

This paper from Niigata, Japan, describes tests done by an unusual method. Agar, containing nothing but salts, was inoculated with *Escherichia coli* and poured into plates. Disks were then cut from it and placed in solutions of chloramphenicol for 20 hours. They were then placed on strips of blotting-paper connecting 2 tanks containing phosphate buffer one above the other between which an electric current was passed; the antibiotic was thus removed from the disk, which was then placed in nutrient broth and incubated; the colonies developing were stained with carbol fuchsin and photographed. When the chloramphenicol was dissolved in buffer solution it had a bactericidal effect at 37°C. (not at 4°), slight up to a concentration of 10 and complete in one of 50 μgm. per ml. When the solution also contained any of various amino-acids and proteins, this bactericidal action was much reduced and incomplete even when the chloramphenicol concentration was 500 μgm. per ml. Carbohydrates had no such interfering action. *L. P. Garrod*

BATTERMAN, R. C. & MOURATOFF, G. J. **Experience with Tetracycline Phosphate Complex administered intramuscularly in Geriatric Patients—Effectiveness, Blood Levels and Local Tolerance.** *Antibiotic Med.* New York. 1958, Aug., v. 5, No. 8, 511–16, 1 fig.

This paper begins by saying that in geriatric practice there is need for a form of tetracycline which can be

injected intramuscularly; coma and uncooperativeness are mentioned as reasons for this. A preparation of tetracycline phosphate complex ("Tetrex", Bristol Laboratories Inc.) which can so be administered was used for the treatment of 108 inmates of a chronic disease institution, most of whom were old, doses of 250 mgm. being injected, usually into the buttock, at intervals of 12, 8 or 6 hours for 2–25 and usually >5 days. Infections of the air passages or lungs were the commonest indication and cystitis the next commonest among 7 others. "Clinical control" was complete in three-quarters of the cases. The injections were generally well tolerated, but 6% complained of severe pain or tenderness. The drug was assayed in the blood of 41 patients and the results are presented in some detail; it is concluded that adequate levels are maintained even by administration only twice daily; no cumulative effect was seen beyond the level reached after the fourth dose. *L. P. Garrod*

LINZ, R. & LECOCQ, E. Sur l'effet bactéricide *in vitro* de l'érythromycine. [**On the Bactericidal Effect of Erythromycin** *in vitro*] *C. R. Soc. Biol.* 1958, v. 152, No. 3, 536–9.

The effect of all possible combinations of penicillin, streptomycin, chloramphenicol, tetracycline and erythromycin, as well as of each antibiotic singly, was determined by adding them to broth in concentrations decided by the sensitivity of the organism to each of them, and plating after incubation to see whether the inoculum had been killed. The results obtained with 2 series of strains of different bacterial species are given in tables simply stating the numbers unaffected in all tests, affected only by other antibiotics: affected by erythromycin but also by other antibiotics and finally affected only by erythromycin, alone or in combination. Erythromycin was found to be in the last-named category ("indispensable") for 8 out of 30 organisms in the first series: these were 15 strains of *Staphylococcus pyogenes*, 1 of *Escherichia coli*, and 2 of *Klebsiella pneumoniae*, and 9 out of 46 in the second series, consisting entirely of Gram-negative bacilli: these were 8 strains of *E. coli* and 1 of *K. pneumoniae*. [The concentrations of erythromycin used were usually from 3 to 50 and sometimes 200 μgm./ml. The higher concentrations in this range are quite unattainable in the body as a whole.] *L. P. Garrod*

ENGLISH, A. R. & FINK, F. C. **Indications for the Usefulness of Triacetyloleandomycin in Epidemic Staphylococcal Infections.** *Antibiotics & Chemotherapy.* New York. 1958, Aug., v. 8, No. 8, 420–23, 2 figs.

Although the term triacetyloleandomycin is used in the title, text and even the 2 figures in this paper, the experiments described were in fact made with oleandomycin base. These consisted of determining the minimum inhibitory concentrations of 4 antibiotics for 64 strains of antibiotic-resistant staphylococci recently isolated in hospitals in the United States. Inhibition by 3·12 μgm. per ml. or less being arbitrarily adopted as the limit of sensitivity, only 3 strains were sensitive to penicillin, 16 to erythromycin, 34 to chloramphenicol but 50 to oleandomycin. [The limit adopted is near that normal for chloramphenicol; hence it is not surprising that 30 strains should be made to appear resistant to this antibiotic. The only finding of interest is that the strains resistant to erythromycin may be sensitive to oleandomycin, and this has been reported before.] *L. P. Garrod*

ENGLISH, A. R. & MCBRIDE, T. J. **Triacetyloleandomycin: Biological Studies.** *Antibiotics & Chemotherapy.* New York. 1958, Aug., v. 8, No. 8, 424–8.

Triacetyloleandomycin has the advantages of acid stability, lack of objectionable taste and better absorption than the parent compound. It is apparently decomposed in some way after oral administration and acts as oleandomycin. This paper reports the minimum inhibitory concentrations *in vitro* of the 2 substances for a variety of bacteria [the triacetyl compound has about one-quarter of the activity of oleandomycin] and the results of therapeutic tests in mice inoculated with 7 strains of staphylococci resistant to various other antibiotics and treated with a single oral dose of triacetyloleandomycin, erythromycin, chloramphenicol, penicillin or novobiocin 30 minutes after intraperitoneal inoculation. The 50% curative dose of triacetyloleandomycin varied from 41 to 105 mgm. per kgm., and that of other antibiotics from 33 to 170 mgm. per kgm., or >200 mgm. per kgm. for an antibiotic to which the strain was resistant *in vitro*. [These experiments would perhaps have been more realistic if more than 1 dose had been given and the period of observation extended beyond 4 days.] Finally, both forms of oleandomycin and the other antibiotics used in these therapeutic experiments were given orally to dogs and assayed in the blood after 1, 3, 5 and 7 hours; in these and similar tests in mice triacetyloleandomycin attained somewhat higher levels than any of the other drugs and these levels were better sustained.
L. P. Garrod

KOCH, Marie L. & LEPLEY, D., Jr. **A Report on Incidence of Coagulase-Positive "Hospital" Staphylococci exhibiting Cross Resistance between Erythromycin and Oleandomycin.** *Antibiotic Med.* New York. 1958, Sept., v. 5, No. 9, 549–52.

This report concerns 451 strains of staphylococci isolated during the first half of 1957 in a general hospital of 1,233 beds where erythromycin is extensively used (700–800 250 mgm. tablets daily) and oleandomycin is not used at all. Of these strains 90 were resistant to erythromycin and 50 to both. The distribution of these types of resistance was similar in strains from infected patients (284) and those from members of the staff who were carriers (167). There was thus at this period a rather more than 50% chance that a staphylococcus resistant to erythromycin would be resistant to oleandomycin as well, despite the fact that the latter drug was not in use.
L. P. Garrod

MARAL, R. & CIACCIO, G. Action de la spiramycine (5.337 R.P.) sur l'infection de la souris par l'agent de la psittacose et sur le développement de la psittacose dans l'embryon de poulet. [**Action of Spiramycin (5.337 R.P.) on Psittacosis Virus in Mice and in Embryonated Eggs**] *C.R. Soc. Biol.* 1958, v. 152, No. 1, 49–52. [16 refs.]

Tested in the embryonated egg and in the white mouse, spiramycin proved as effective as chlortetracycline against psittacosis virus. *S. P. Bedson*

MIYAKAWA, T., ANZAI, O. & SHIMIZU, N. **Studies on Antiviral Antibiotics from *Streptomyces*. VIII. Various Antibiotics as Inhibitors of Influenza Virus in Tissue Culture.** *Japanese J. Microbiol.* 1958, Jan., v. 2, No. 1, 53–62, 1 fig.

The reagents used in these experiments were 28 known antibiotics and 7 others recently isolated by the authors. They were added to tissue cultures of chorioallantoic membrane inoculated with the PR8 strain of influenza virus and their effect on virus multiplication was judged by subsequent haemagglutinin titration. Observations were also made on the effect of the antibiotics on the tissue itself (test for glucose dehydrogenase activity made with tetrazolium salt), on direct inactivation of the virus in the absence of tissue, and on the effects of treating the tissue with antibiotic before inoculating it with the virus. The most promising of the antibiotics tested was one of the new ones, myxoviromycin, and since this was without effect in all the subsidiary tests mentioned, it is believed to act by inhibiting intracellular virus multiplication.

L. P. Garrod

HINUMA, Y., SATO, S., CHIBA, M., IKEDA, T., MIYAKAWA, T. & MIZUNO, H. **Studies on Antiviral Antibiotics from *Streptomyces*. IX. The Inhibitory Effect of several Antibiotics on the Growth of Influenza Virus in Embryonated Eggs and in Mice.** *Japanese J. Microbiol.* 1958, Jan., v. 2, No. 1, 63–8. [13 refs.]

The 7 new antibiotics referred to in the preceding paper together with 6 others there shown to inhibit the growth of influenza virus *in vitro* were tested by 2 *in vivo* methods. The maximum tolerated dose was injected into the allantoic cavity of the chick embryo and intraperitoneally into mice inoculated intranasally, and virus was subsequently titrated in allantoic fluid and lung respectively. 7 of the antibiotics inhibited virus growth in the chick embryo and only 3 in the mouse: these were myxoviromycin, E-150 (another new substance) and thiolutin, but the 2 latter also exhibited toxicity (nature unspecified), thus leaving myxoviromycin as the only substance "eligible for further chemotherapeutic study". *L. P. Garrod*

NOUFFLARD, H. & BERTEAUX, S. Activité antituberculeuse du produit B-663. [**Antituberculous Action of B-663**] *Ann. Inst. Pasteur.* 1958, Oct., v. 95, No. 4, 449–55.

BARRY and his collaborators have reported [this *Bulletin*, 1957, v. 32, 945] that B-663 has high antituberculous activity *in vitro* and *in vivo*, and in this paper the authors report experiments which confirm these claims.

In the *in vitro* tests, which were done in Dubos albumin-oleic-acid medium, B-663 inhibited the growth of H37Rv and the Ravenel strain at a concentration similar to that of isoniazid; it also inhibited a highly isoniazid-resistant strain.

In the *in vivo* tests in mice the activity shown by 100 μgm. B-663 per kgm. was at least equal to that of the same dose of isoniazid; the treatment in these tests was started either on the 1st or the 14th day of infection, but a depot effect of B-663 was also confirmed. The antituberculous activity was shown to continue for many days after dosing was stopped and to be apparent with intermittent therapy starting the day before infection and lasting for 3 weeks, *i.e.* on alternate days, once a week, twice or 3 times during the period or even when given only on the day before infection.

S. R. M. Bushby

LEVY, H. B. & HAAS, V. H. **Alteration of the Course of Lymphocytic Choriomeningitis in Mice by certain Antimetabolites.** *Virology.* New York. 1958, June, v. 5, No. 3, 401–7. [10 refs.]

These observations originated in the chance discovery of lymphocytic choriomeningitis virus in leukaemic mice, following which it was shown that treatment with amethopterin protects mice against intracerebral inoculation with this virus, but without preventing multiplication of the virus, which indeed is found in the blood and viscera when it is not demonstrable there in untreated controls. This paper reports that 3 other anti-metabolites, 5-fluorouaracil, azaserine and 6-diazo-5-oxo-nor-1-leucine have a similar protective action but less efficient than that of amethopterin, that treatment with amethopterin or azaserine causes virus to persist in the blood of mice inoculated subcutaneously, and that the protective action of amethopterin is reduced but not abolished by administering certain purines and pyrimidines. *L. P. Garrod*

COLOBERT, L., with the technical collaboration of A. CAVANAGH, J. GUILLOU & Marie T. HAMON. Étude de la lyse de salmonelles pathogènes provoquée par le lysozyme, après délipidation partielle de la paroi externe. [**Study of Lysis of Pathogenic Salmonellae induced by Lysozyme after Partial Delipidation of the External Wall**] *Ann. Inst. Pasteur.* 1958, Aug., v. 95, No. 2, 156–67, 2 figs. [32 refs.]

These experiments were made with typhoid and paratyphoid (A and B) bacilli. Lysozyme was without effect on these organisms unless they had previously been immersed in an ampoule in boiling water for 10 minutes (lytic changes then only demonstrable by electron microscopy), or treated with Teepol or the sodium salt of ethylenediamine tetra-acetic acid. Since these treatments would have the effect of removing lipids, it is suggested that a substrate in the cell wall on which lysozyme acts is exposed when this has occurred. It is also reported that unduly high concentrations of lysozyme fail to cause clearing of a

suspension of acetone-dried *Micrococcus lysodeikticus*; on the contrary its opacity may increase.

L. P. Garrod

WORSECK, M. Prüfung der bakteriziden Eigenschaften einer belgischen UV-Lampe. [**Tests of the Bactericidal Properties of a Belgian Ultraviolet Lamp**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Jan.–Feb.–Mar.–Apr., v. 4, Nos. 1/2, 1–15, 7 figs. [29 refs.]

After a long discussion of the literature on the use of ultra-violet irradiation for disinfection, the authors describe the characteristics of a tubular low-pressure mercury lamp made by Westinghouse. This they tested by exposing culture plates, previously inoculated with known numbers of staphylococci, coliform and spore-bearing bacilli, for various times at 15 cm. from the lamp. More than 99% of all the strains tested were killed in 45 seconds but complete sterilization of the plates took much longer, not always being complete by 15 minutes. The lamp is considered suitable for use in a media-preparation room.

R. E. O. Williams

AMANO, T., GOEBEL, W. F. & SMIDTH, Elizabeth M. **Colicine K. III. The Immunological Properties of a Substance having Colicine K Activity.** *J. Exper. Med.* 1958, Nov. 1, v. 108, No. 5, 731–52, 1 text fig. & 2 figs. on 2 pls. [19 refs.]

"By immunological means it has been shown that colicine K is associated with the O antigen of the colicinogenic bacillus *E. coli* K_{235} L+OC+.

"The colicine K–O antigen complex elicits the formation of at least two types of antibodies, one a precipitin, the other colicine-neutralizing antibody. The first precipitates colicine K without neutralizing it, the second neutralizes the coline without precipitating it.

"Unlike the purified colicine K complex, the colicine protein component of the O antigen is precipitable by the neutralizing antibody.

"There is no demonstrable serological relationship between colicine K and phage T_6. These two agents must be considered to be separate and distinct entities."

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order:—General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

GRANT, L. S., GRACEY, L. & CLARK, Betty M. **The Prevalence of *Salmonella, Shigella* and Typhoid Phage Types in Jamaica.** *West Indian Med. J.* 1957, Dec., v. 6, No. 4, 233–6.

During the period 1952–56 the most common salmonella found in Jamaica was *Salmonella typhi.* It comprised 1,475 of 2,011 strains (73·3%) and the next most common, *Salm. typhi-murium,* comprised only 194 (9·6%). *Salm. paratyphi B* has not yet been encountered. In general, the distribution of salmonella strains was similar to that of the U.S.A. Only 4 phage types of *Salm. typhi* were found in 738 strains examined. They were E1 (56·1% of foci), T (19·2%), C (6·0%) and A (2·8%).

The most common shigellas were *Shigella sonnei,* which accounted for over half the strains examined, and *Sh. flexneri.* The most frequent type of the latter was *Sh. flexneri* III (Z). *J. Nagington*

SPANÒ, C. Sopra un nuovo tipo fagico Vi di *S. typhi.* [**A New Vi Phage Type of *Salmonella typhi***] *Riv. Istituto Sieroterap. Ital.* 1958, July–Aug., v. 33, No. 4, 288–90.

An additional phage type of *Salmonella typhi* has been demonstrated by the technique of CRAIGIE and YEN of adapting strains to the Vi 2 phage.

The new phage obtained, which is called "Puglisi" on account of the place of its origin in Sicily, only gives confluent lysis with the type A and the homologous strain but a few plaques may appear with type 29. The only Vi phages which give any considerable reaction with the strain Puglisi are E7 and F 2.

These findings have been confirmed by E. S. ANDERSON of London and P. NICOLLE of Paris and the latter has observed strains closely corresponding which have come from Tunisia. It is suggested that this organism should appear as Type 42 in the Craigie/Felix scheme.

J. W. McLeod

LIPP, R. & IHM, P. Ein quantitativer Bakteriämietest an der Maus zur Bewertung der Typhus-Impfstoffe und -Sera. [**Assessment of Products designed to give Active or Passive Immunity to Typhoid Infection by a Quantitative Determination of Bacteriaemia in the Mouse after Infection**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 1, 14–25, 5 figs. [Numerous refs.]

A review of the published work with regard to the efficacy of immunization against enteric infection reveals doubts in some quarters about the superiority claimed for preparations depending on Vi antigen [this *Bulletin,* 1957, v. 32, 836; 1958, v. 33, 508 *bis*]. The authors think, therefore, that further "field trials" are required to clear up this point. Meanwhile they suggest that a substitute should be introduced for the experimental assessment of the value of various antigens and antisera by their success in controlling the effect of a dose of bacteria capable of causing the death of 50% of injected mice. This is the intraperitoneal injection of a dose of bacilli 10 times less than that required to give 50% mortality and the determination of the numbers of bacteria which appear in the blood 15–30 minutes after injection, expressed as a percentage of the number appearing in the control.

The Vi active strain Ty 2 was used and 10 million were injected intraperitoneally in such tests.

The statistical significance of results obtained in this way is discussed.

The advantages claimed for the method are the use of a smaller dose so that there is better differentiation between invasive and toxic effect and also the possibility of finer grading of the protective effect of various antigens and antisera. *J. W. McLeod*

ADLER, F. Endemische Verseuchung des Personals von Lebensmittelbetrieben mit Salmonella Blockley. [**Endemic Infection of Personnel in the Food Industry with Salmonella Blockley**] *Desinfektion u. Gesundheitswesen.* 1958, Sept.–Oct., v. 50, Nos. 9/10, 130–33.

In this paper reference is first made to the observation that during the past years the rarer salmonellae have come to be recognized as the cause of infections more and more frequently in Germany, whereas there has been a definite reduction in the numbers of cases of typhoid and paratyphoid. Salmonella Blockley [this *Bulletin*, 1956, v. 31, 193] was first isolated in Germany from the faeces of a patient with enteritis in February 1955 and later in that year caused an epidemic of 2,000 cases of severe enteritis with 3 deaths, and was also isolated in 16 other localities. Since that time Salm. Blockley has been found in the investigation of a considerable number of outbreaks details of which are given [see, for example, *ibid.*, 1956, v. 31, 860]. A number of food handlers have been found to be healthy carriers of the organism which has also been isolated from a number of meat foods such as sausages of various kinds and ham. The organism was also isolated from the faeces of starlings which had probably ingested the organism from the area of a sewage works. The prevention of infection with Salm. Blockley is discussed with particular reference to the adequate bacteriological examination of food handlers, close cooperation within the medical profession and between it and veterinarians.
M. E. Delafield

NAVA, G. C. & BO, G. Sulla composizione chimica degli antigeni delle Salmonelle. V. Composizione chimica degli antigeni somatici delle salmonelle Aberdeen, Luciana, Veneziana, Gaminara e Memphis. [**Chemical Composition of Salm. Aberdeen, Luciana, Veneziana, Gaminara and Memphis**] *Riv. Italiana d'Igiene.* 1958, May–June, v. 18, Nos. 5/6, 200–208. [14 refs.] English summary.

Boivin's method of extraction with trichloracetic acid was used in preparing these antigens and the sugars and amino sugars present in these fractions were subjected to chromatographic analysis.

The chief result obtained was to show that, where the somatic antigenic grouping differed, chromatographic analysis indicated a difference in the sugars or amino sugars or both; but it was also found that, even where the antigenic factors were similar and strains within a group showed a similar qualitative composition in respect of sugars present, they still differed in the relative quantities in which these sugars occurred. This was notable with the strains Hvittingfoss and Gaminara, both belonging to group 16 but diverging widely in their galactose content. *J. W. McLeod*

FORMAL, S. B., LOWENTHAL, J. P. & GALINDO, Emma. **Serological Study of the Mucinases from** *Shigella flexneri*. *J. Bacteriology.* 1958, Apr., v. 75, No. 4, 467–70.

In a previous study FORMAL and LOWENTHAL [this *Bulletin*, 1956, v. 31, 1257] could find demonstrable amounts of mucinase produced only by *Sh. flexneri* strains 2a, X and Y.

The mucinolytic activity of mucinase preparations was measured by their ability to depolymerize ovomucin so that it could not be precipitated by cetyl trimethylammonium bromide (CTAB). Antisera to mucinase were titrated by their ability to inhibit the mucinolytic action of a fixed quantity of mucinase.

The sera of rabbits immunized with mucinase were found to give approximately the same titre in each case against the homologous mucinase, *i.e.* 1 : 640. The mucinases of *Sh. flexneri* 2a, X and Y were serologically related. They were not related either to the mucinase of *Vibrio cholerae* or to that of a strain of *Escherichia coli* of Group O 17. *J. Nagington*

JUNGHANS, Ruth. Ergebnisse der Lysotypie von *Shigella sonnei* Stämmen in Berlin in den Jahren 1955 bis 1957. [**Results of Phage Typing of** *Shigella sonnei* **Strains isolated in Berlin in 1955 to 1957**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 50–54, 2 figs.

The English summary appended to the paper is as follows:—

"2070 Sh. sonnei strains, isolated in 1955, 1956 and 1957, were typed with test phages of Hammarström using his technique. The results of Hammarström could be confirmed. All types found in both preceding years could be detected again in 1957. Their relative frequency has changed every year."

WILEY, B. B. & SCHERP, H. W. **Capsular Polysaccharides of** *Escherichia coli*, **Types K28A and K34A.** *Canadian J. Microbiol.* Ottawa. 1958, Oct., v. 4, No. 5, 505–16. [35 refs.]

DAVIS, Betty R. & EWING, W. H. **Six New** *Escherichia coli* **H Antigens, H41 to H46.** *Canadian J. Microbiol.* Ottawa. 1958, Oct., v. 4, No. 5, 517–19.

DI GIROLAMO, M., MAGLIOCCO, F., SCHIESSER, A. & TECCE, G. Utilizzazione del D-arabinosio in *Escherichia coli*. [**Utilization of D-Arabinose in** *Escherichia coli*] *Giorn. di Microbiol.* Naples. 1958, Mar.–Apr., v. 5, No. 2, 111–26, 5 graphs. English summary.

MACDONALD, R. E. & GERHARDT, P. **Bacterial Permeability: the Uptake and Oxidation of Citrate by** *Escherichia coli*. *Canadian J. Microbiol.* Ottawa. 1958, Apr., v. 4, No. 2, 109–24, 4 figs. [29 refs.]

VOLKIN, E., ASTRACHAN, L. & COUNTRYMAN, Joan L. **Metabolism of RNA Phosphorus in *Escherichia coli* infected with Bacteriophage T7.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 545–55, 3 figs. [23 refs.]

UMBARGER, H. E. & BROWN, Barbara. **Isoleucine and Valine Metabolism in *Escherichia coli.* VIII. The Formation of Acetolactate.** *J. Biol. Chem.* 1958, Nov., v. 233, No. 5, 1156–60, 4 figs. [19 refs.]

BERNSTEIN, I. A. & SWEET, Dorothy. **Biosynthesis of Deoxyribose in Intact *Escherichia coli.* *J. Biol. Chem.* 1958, Nov., v. 233, No. 5, 1194–8, 2 figs. & 1 diagram. [26 refs.]

BERNSTEIN, I. A., FOSSITT, D. & SWEET, Dorothy. **Bacterial Degradation of Deoxyribose-C^{14}.** *Ibid.*, 1199–1202, 2 diagrams. [14 refs.]

WADE, H. E. & LOVETT, S. **The Incorporation of Phosphorus into Fractions of *Escherichia coli* made by Centrifuging and by Chemical Means.** *Biochem. J.* 1958, Dec., v. 70, No. 4, 697–705, 3 figs. [Numerous refs.]

IWAMURA, N. **Studies on the *coli-aerogenes* Group (10). Effects of Environmental Factors on the Nature of *Escherichia coli.* I. Alteration of the Formic Hydrogenlyase Activity of *Escherichia coli* in the Case of the Environmental Change from Feces to Water.** *Yonago Acta Medica.* 1958, Sept., v. 3, No. 2, 96–103, 5 figs. [22 refs.]

Potential formic hydrogenlyase (FHL) activities of *Escherichia coli* in faeces and water have been studied. FHL is adaptive and readily inactivated. The author has attempted to determine the potential FHL activity of *E. coli* in nature. The most successful method for this purpose was the determination of the adaptive enzyme activities of non-proliferating cells prepared under aerobic conditions from sugar-free media. It is most important to avoid the use of fermentative sugars in this work.

It was possible to distinguish the difference between the FHL activity of *E. coli* isolated from faeces and from water, and the amount was remarkably lower in the latter.

When *E. coli* from faeces were stored in water, the longer the period, the lower the degree of FHL activity. The correlation between this decreasing activity and the length of storage was significant.

E. Windle Taylor

MCRORIE, R. A. & NOVELLI, G. D. **Glucuronate Metabolism by *Aerobacter aerogenes.*** [Correspondence.] *Nature.* 1958, Nov. 29, v. 182, 1504–5.

LARK, K. G. **Abnormal Growth induced by Penicillin in a Strain of *Alcaligenes fecalis.*** *Canadian J. Microbiol.* Ottawa. 1958, Apr., v. 4, No. 2, 165–77, 7 figs. (2 on 2 pls.) [10 refs.]

LARK, K. G. **Variation during the Cell-Division Cycle in the Penicillin Induction of Protoplast-Like Forms of *Alcaligenes fecalis.*** *Canadian J. Microbiol.* Ottawa. 1958, Apr., v. 4, No. 2, 179–89, 4 figs. [11 refs.]

OEHRING, H. & SCHABINSKI, G. Experimenteller Beitrag zur Frage der Toxizitätssteigerung der Diphtheriebakterien im tierischen Organismus. **[Experimental Observations on Increased Toxicity of Diphtheria Organisms in Animal Passage]** *Ztschr. f. ärztl. Fortbildung.* 1958, Sept. 1, v. 52, Nos. 17/18, 776–83, 3 figs. [40 refs.]

This communication reveals the still considerable incidence of diphtheria infection in some parts of Germany. In the public health laboratory of Jena 302 diphtheria strains were isolated from 230 individuals in a period of 18 months beginning in September 1956. From these, 117 strains were selected for special investigation. These comprised 14 *gravis* strains (10 from cases of diphtheria, 3 from carriers and 1 from a case of chronic rhinitis); 94 *mitis* strains (4 from cases of diphtheria, 48 from carriers, 11 from chronic rhinitis and the rest from other conditions of which 19 were unspecified); and 9 *intermedius* strains (3 from mild cases of diphtheria, 5 from carriers and 1 unspecified).

All the *gravis* strains were toxin positive both by the Römer test and the Ouchterlony plate and in the latter mostly with the highest concentration of antiserum used. Of the *mitis* strains 63 were positive by Römer test but only 29 of these in the Ouchterlony plate. Of the *intermedius* strains 7 were positive by the Römer test and 7 by the Ouchterlony plate but 1 negative by the first test was positive by the second.

The most interesting and the original part of this investigation was an attempt to pass strains through a succession of guineapigs by recovering the strains from the intracutaneous lesions and, after purification, passing the strain recovered to a second and successive guineapigs. The results so obtained were that 10 out of 14 *gravis* strains survived 5 passages. 16 out of 94 *mitis* strains were recovered after 5 passages but none of the 9 *intermedius* strains.

The most noteworthy finding was that after one or more passages the *mitis* strains showed augmented toxin production. The evidence of this was more extensive lesions in the guineapig and positive results in the Ouchterlony plates with higher concentrations of antitoxin.

This result was obtained in several instances with strains negative either by the Römer or by the Ouchterlony techniques and in 2 instances with strains negative by both methods.

It is therefore possible to confirm by other methods the observations on conversion of atoxic to toxin-forming strains under the influence of bacteriophage [FREEMAN & MORSE, this *Bulletin*, 1952, v. 27, 968].

The obvious conclusion is drawn that strains of *Corynebacterium diphtheriae* found atoxic by the usual methods cannot be discounted as harmless. A number of discrepancies between the results of the Römer and the Ouchterlony tests were observed and some strains negative by both tests were found to be toxin producers when subjected to the more delicate test of Jensen on the skin of the rabbit. *J. W. McLeod*

SENAY, L. C., Jr., ENZINGER, F. & HINES, H. M. **Production of Dystrophic Lesions in Skeletal Muscles of Dutch Rabbit by Diphtheria Toxin.** *Arch. Pathology.* 1958, Sept., v. 66, No. 3, 344–51, 5 figs. [14 refs.]

The muscles studied were the diaphragm and gastrocnemius. For the diaphragm studies animals were given toxic filtrate intraperitoneally and then killed and examined 8, 12 and 20 hours and 6, 12 and 20 days later. Control animals receiving no injection were killed and examined at various times during the course of the experiment, and controls which received antitoxin-neutralized toxin were killed and examined 6 days after injection. The maximum isometric tetanus tension and the fatigue time were determined for a slip of diaphragm and the tension was calculated on the basis of the wet muscle weight. The adrenals were weighed and one adrenal and the heart were examined histologically. On the 6th day after toxin administration the mean tension values showed a 45% decrease compared with controls, and improvement was not shown at either 12 or 20 days. The fatigue times did not differ significantly from those of controls. The first histological changes in the diaphragm were seen at 24 hours and were more severe at 6 days. Cross striation was lost first, then the involved fibres became swollen and later fragmented. This process was accompanied by sarcolemmal nuclear proliferation and the appearance of macrophages. This reaction sometimes surrounded islands of necrotic tissue. After removal of necrotic tissue, regeneration began but was incomplete owing to the occurrence of fibrosis. Fatty degeneration was not conspicuous. Cardiac lesions were similar to, but less extensive than, diaphragmatic lesions. No changes occurred in muscles from animals injected with neutralized toxin. At 6 days adrenal hypertrophy was present but no necrosis was observed.

Diphtheria toxin had no effect *in vitro* on the twitch height of normal diaphragm slips.

For gastrocnemius studies animals were given 1, 2 or 3 injections of toxin, with 2 days between injections. All animals were tested 6 days after the first injection. The maximum isometric tetanus tension values did not differ significantly from those of the controls, but the fatigue time was significantly decreased in the group receiving 3 injections of toxin. Adrenal weights in this group were all significantly increased compared with controls.

Many fewer muscle fibres in the gastrocnemius showed degeneration than in the diphragms of these rabbits.

The early onset of lesions would appear not to be due to nervous system damage. The lesions resembled those seen in experimental muscular dystrophy except for the greater fibrous replacement noted.

R. J. Fallon

ANDERSON, P. S., Jr. & COWLES, P. B. **Effect of Antiphage Serum on the Virulence of** *Corynebacterium diphtheriae.* *J. Bacteriology.* 1958, Sept., v. 76, No. 3, 272–80. [24 refs.]

Working with an indicator strain, C4, a temperate phage β active against it and a virulent phage B derived from the last, the authors succeeded in producing a serum active against both phages. This was done by injection to rabbits previously immunized with diphtheria toxoid of B phage of high potency—titre 10^9–10^{10}.

When a toxigenic C4 strain carrying the β phage was transmitted serially day after day in 5% of such serum in broth, it was found after 107 passages to have lost all lysogenicity, whereas control cultures in broth prepared with normal serum had not.

In vivo tests in which animals injected with considerable doses of toxigenic C4 culture carrying β phage and given sufficient antitoxin to allow of development of a lesion and survival of the animal showed that nontoxigenic strains could be recovered from these lesions and that simultaneously the sera of the animals had developed phage-neutralizing capacity. It is suggested that the development of antiphage immune bodies in the serum may account for conversion of toxigenic to atoxigenic strains within a patient's body.

J. W. McLeod

KRANZDORF, H. & BANC, S. Contribution à l'étude des méthodes de purification des anatoxines. I. Purification de l'anatoxine diphtérique à l'acide métaphosphorique. **[Study of Methods of Purification of Toxoids. I. Purification of Diphtheria Toxoid by Metaphosphoric Acid]** *Arch. Roumaines Path. Exper. et Microbiol.* 1957, Dec., v. 16, No. 4, 579–86.

The authors draw attention to the superiority of metaphosphoric acid to other acid precipitants in the purification of diphtheria toxoid. This is due to the combination of the acid radicals of the metaphosphoric acid with the basic protein groups with formation of compounds insoluble in the *p*H range 1·0–4·0.

If a preliminary precipitation with H_2SO_4 or CCl_3-COOH is carried out for 24 hours at *p*H 4·0–4·15 and the supernatant is then precipitated with metaphosphoric acid at *p*H 3·2, a product of 2,200 Lf./mgm.N may be obtained. *J. W. McLeod*

VIALLIER, J. & CAYRÉ, R. M. Difficultés actuelles de l'identification des Mycobactéries. **[Current Difficulties in the Identification of Mycobacteria]** *C.R. Soc. Biol.* 1958, v. 152, No. 1, 109–12.

The authors recommend that the cultures be examined for isoniazid and PAS resistance, catalase activity, pathogenicity for guineapigs, hamsters, rats and mice, reduction of methylene blue and fixation of neutral red.

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In their drug-sensitivity tests they use the Youmans medium plus horse serum, and the strains growing as dispersed growth are suspected of being non-pathogenic mycobacteria. The use of hamsters is valuable as only virulent tubercle bacilli produce lesions, *e.g.* not BCG.

Of the 2 dye tests recommended, the neutral red test is the more valuable especially with BCG strains as these stain a specific carmine hue. The methylene blue test is of limited value and depends partly on the growth stage of the culture, but with actively growing bacilli it is strongly positive with the non-pathogenic mycobacteria. *S. R. M. Bushby*

HIRSCH, A. & CATTANEO, C. Die Mycobakterien: Chemischer Aufbau und Virulenz. III. Die Reduzierung von Triphenyltetrazoliumchlorid durch Mycobakterienstämme verschiedener Species. **[Mycobacteria: Chemical Structure and Virulence. III. Reduction of Triphenyltetrazolium Chloride by Various Species of Mycobacteria]** *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 1, 71–84, 2 figs. [Numerous refs.]

The findings of the authors are that the reduction of the tetrazolium salt, which is colourless, to the red-coloured compound formazan by mycobacteria is considerably influenced by the reaction of the mixture. In alkaline conditions most mycobacteria will reduce it but in acid conditions only the saprophytic forms do so. There is good correlation, therefore, between virulence, failure to reduce tetrazolium and the persistence of a relatively positive redox potential.

The technique recommended is the use of Sørensen phosphate buffer mixture at a *p*H level of 5; in 100 ml. of this 0·025 gm. of 2–3–5 triphenyltetrazolium chloride are dissolved (the reagent will remain active for a week if kept cold in the dark). 0·5 ml. amounts of it are mixed with about 5 mgm. of massed mycobacteria and thoroughly mixed. Readings are taken after 60 minutes at room temperature. No colour = negative result; rose colour = dubious result; red colour = positive result; purple to violet colour = strong positive result.

J. W. McLeod

COOK, G. T. **Isolation of Tubercle Bacilli from Homogenized Sputum before and after Concentration.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Sept., v. 17, 219–21.

This paper compares the results of culturing 1,872 specimens of alkali-treated sputum, before and after centrifuging. An equal volume of sodium hydroxide was added to the specimen, and after 30–45 minutes at 37°C. 1 loopful of the mixture, without neutralization, was inoculated on to a Löwenstein-Jensen slope. The mixture was then centrifuged for 15 minutes at 3,000 r.p.m. and a loopful of the deposit inoculated on to another tube of the medium.

The deposits of 1,778 of the specimens contained no acid-fast bacilli in direct films, and from these tubercle bacilli were grown from the deposit and the uncentrifuged alkali mixture of 46, from only the uncentrifuged mixture of 6, and from only the deposit of 59. On 2 occasions 1 of the corresponding cultures was contaminated. The remaining 94 were microscopically positive and all grew tubercle bacilli, 89 in both cultures, 1 on the culture from the uncentrifuged specimen (the slope inoculated with the deposit was contaminated) and 4 only in the culture from the deposit.

Thus with specimens in which the tubercle bacilli were scanty a higher percentage of positive cultures was obtained from the deposit, and moreover when the number of colonies growing on the slopes of specimens from which both cultures were positive were compared, the heavier growth was found in the culture from the deposit. However, as the contamination rate in the cultures before centrifuging was 0·6% as compared with 3·9% in those from the deposit, the author recommends that when the specimens are suspected of containing many tubercle bacilli, an additional tube of medium inoculated before centrifuging may be of value if the culture from the deposit proves to be contaminated. *S. R. M. Bushby*

LITTLE, L. A. & DEVINE, J. M. **The Effect of Centrifugation on the Cultivation of Tubercle Bacilli from Sputum.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Oct., v. 17, 239–42.

Smears of the sputa were examined by fluorescence microscopy for acid-fast bacilli and those containing 1–3 bacilli per low-power field were classed as "scanty positive". An equal volume of N NaOH was added to the remainder of the specimen, placed in the incubator at 37°C. for 15 minutes and shaken at intervals. 2 Löwenstein-Jensen slopes were then inoculated from each of the mixtures, 1 loopful (6 mm.) being used from each of the first 960 of the 1,556 specimens and 3 loopfuls from the remainder, but as on analysis the results of both inocula did not differ, they are compounded in this report. 5 minutes after making these inoculations the mixtures were diluted by half-filling the bottles with distilled water and then centrifuging for 30 minutes at 3,000 r.p.m. Some of the deposits were resuspended in 0·5 ml. distilled water before being neutralized, in which case 0·25 ml. was inoculated on to 2 Löwenstein-Jensen slopes, 3 loopfuls being used when the dilution in 0·5 ml. distilled water was omitted.

1,392 specimens were negative by direct film and of these, 104 were positive by culture, 63 being positive by both methods, 30 from the deposit alone and 11 from the uncentrifuged specimen alone. 53 specimens were "scanty positive" by direct film and 49 of these were positive by culture, 46 being positive by both methods and 3 from the uncentrifuged specimen only. 111 specimens were strongly positive by direct smear and all of these were positive by culture, 1, however, being positive from the deposit alone and 9 being positive from the uncentrifuged specimen alone.

The contamination rate was higher with cultures from the deposit—4·8% as compared with 2·5%, and

of the 12 deposits from which tubercle bacilli were not grown but which were grown from the corresponding uncentrifuged specimen, 7 were contaminated.

These results show that nothing is to be gained by centrifuging microscopically positive sputa but that there is a need for centrifuging microscopically negative specimens. *S. R. M. Bushby*

CRONE, P. B. **Culture of Tubercle Bacilli from Treated and Untreated Patients.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Sept., v. 17, 221–4.

Because of an apparent increase in recent years in the number of specimens of sputum from treated patients containing acid-fast bacilli in stained films but from which no tubercle bacilli could be grown, the author kept a special watch from September 1956 to May 1957 for specimens of this type.

During this period, of the 28 specimens with positive smears from untreated patients which yielded at least 1 uncontaminated culture, only 1 failed to grow tubercle bacilli, and from 219 similar specimens from treated patients, 28 failed to grow the bacilli. However, these differences are not statistically significant, but when the time of incubation that the cultures took to become positive is taken into account, a longer period is seen to be necessary with the specimens from the treated patients. Also, each of the specimens was cultured on 2 slopes of Löwenstein-Jensen medium and when comparison was made of the incidence of cultures positive on only one of the slopes, the other being uncontaminated, more were found among those from the treated patients, a finding which again indicates that these bacilli are more difficult to grow.

These results are in agreement with those of COLLARD *et al.* [this *Bulletin,* 1953, v. 28, 911]. *S. R. M. Bushby*

VIALLIER, J. Traitement par les ammoniums quaternaires des produits pathologiques pour l'isolement du bacille tuberculeux. **[Treatment of Pathological Material with Quaternary Ammonium Compounds for the Isolation of Tubercle Bacilli]** *Ann. Biol. Clin.* 1956, Oct.–Dec., v. 14, Nos. 10/12, 722–3.

The compound used is methyl phenyl dodecyl trimethyl ammonium methosulphate (Desogen). 2 cc. of sputum or other material are mixed with 2·5 cc. of 1 in 1,000 Desogen and left for 90 minutes after preliminary shaking, at the end of which time the mixture is centrifuged for 10 minutes at over 5,000 r.p.m., and the sediment is washed twice in sterile distilled water, and sown on media.

540 sputa were treated in this way and also by the sulphuric acid technique; 114 were positive with both, 40 were positive with Desogen and negative with sulphuric acid, and 21 were negative with Desogen and positive with sulphuric acid. There is therefore a slight advantage with Desogen, and the technique is easy. *Charles Wilcocks*

VIALLIER, J., AUGAGNEUR, J. & BIOT, N. Résultats de l'isolement du bacille tuberculeux à partir de produits pathologiques par l'emploi de sels d'ammonium quaternaire. Influence de l'association de ferments protéolytiques. **[Isolation of Tubercle Bacilli from Pathological Material after Treatment with Quaternary Ammonium Salts: Effect of Proteolytic Ferments]** *C.R. Soc. Biol.* 1958, v. 152, No. 1, 107–9.

In the first part of this paper the results of treating 3,000 specimens of sputum or mucus from gastric lavage with methyl phenyl dodecyl trimethyl ammonium methosulphate by the method described earlier [above] and with sulphuric acid are compared; the specimens were cultured on Löwenstein medium. 786 of these specimens were positive in direct smear and of these, 703 gave positive cultures and 25 were contaminated after treatment with the quaternary salt, and 681 were positive and 18 contaminated after the acid. Of the 2,214 specimens negative in direct smear, 200 yielded positive and 45 contaminated cultures after treatment with the salt, and 181 gave positive and 6 contaminated cultures after the acid. The salt method therefore gave a high proportion of positive cultures in spite of a higher contamination rate, but in the examination of 310 other pathological specimens, *i.e.* urine, cerebrospinal fluid or resected lung tissue, this superiority was not observed. Growth was usually more rapid on the Löwenstein medium after the salt treatment than after the acid treatment.

Homogenization of the specimen is often incomplete with the salt method and in consequence 500 specimens of sputum and gastric lavage were treated in duplicate by the salt method, 1% pancreatin being added to the salt in one of the examinations. Without the enzyme 144 cultures were positive and 4 were contaminated, and with the enzyme 118 were positive and 5 were contaminated. A similar inferior result was obtained when 1% pepsin was used instead of the pancreatin and the authors conclude that the addition of the enzyme is not an advantage. *S. R. M. Bushby*

SIMPSON, D. M. & REED, R. W. **Slide Culture of Tubercle Bacilli. IV: Further Diagnostic Trials.** *Amer. J. Pub. Health.* 1958, Sept., v. 48, No. 9, 1153–61, 2 figs. [21 refs.]

This is a continuation of the authors' study of this method of culturing tubercle bacilli from sputum. The method is given in detail with a description of the special apparatus for minimizing the risk of infection during the killing of the non-acid-fast bacilli with 6% sulphuric acid and the washing of the slides free from the acid.

The first part of the paper compares the results of examining 7,010 specimens by the slide method with Kirchner medium, with those obtained by the method that has been commonly used in the authors' laboratory for some years; in this latter method the specimen was treated with trisodium phosphate and cultured on Herrold egg-yolk agar medium. Of 482 of the specimens positive by direct smear, 68·1% were positive by both cultural methods, 22% by the slide method

alone and 4·7% by the routine method alone; 5·2% were negative by both methods. Of the remaining 6,528 specimens, negative by direct smear, 1·2% were positive by both methods, 1·0% by the slide method alone and 1·3% by the routine method alone.

The second part of the paper describes the results of examining 200 specimens of sputum from patients who had sporadically yielded positive cultures. These specimens were examined by the slide method and by culturing after concentration by the sodium hydroxide method on to the media of Herrold, Petragnani, Löwenstein, Tarshis (blood) and American Trudeau Society (ATS); each specimen was inoculated on to 2 slides and 2 tubes of each of the media. The concentrates were also injected into 2 guineapigs. Of the conventional media, that of Herrold gave the highest percentage of positive results and the ATS gave the lowest. When the results with the conventional media are consolidated and compared with the slide method and the guineapig method, the slide method proved to be the most efficient with specimens that were positive by a direct-smear of the concentrate, but it was less efficient with negative-smear specimens. In assessing the results by this method it must be remembered that those with the slide method are obtained from duplicate cultures, whereas those from the conventional media are from 10 cultures of each specimen. The actual percentages of the 54 positive-smear specimens yielding a positive result (5 specimens were negative by all 3 methods) were 98·2% by the slide method, 85·2% by the solid media and 76% by guineapig; of the 29 negative-smear specimens yielding a positive result (112 specimens were negative by all 3 methods), 62·1% were positive by the slide method, 72·5% on the solid media and 55·2% by guineapig.

The main advantage of the slide method was the rapidity with which the results were obtained; the slides were examined after 1 and 2 weeks, and at 1 week 45% of the positive specimens of the first study were positive whereas with Herrold medium no specimen was positive at 2 weeks and it was not until 8 weeks that the positive cultures approached 100%.

[For Part III, see this *Bulletin*, 1956, v. 31, 197.]

S. R. M. Bushby

PATERSON, A. B., WRIGHT, E. C. & PATTERSON, D. S. P. **Trace Elements in the Preparation of Tuberculin.** *Tubercle.* 1958, Oct., v. 39, No. 5, 275–82. [24 refs.]

The difficulties of culturing tubercle bacilli for the production of tuberculin have been largely resolved by the addition of the Baisden inorganic salt mixture to synthetic media, and the present work is essentially a confirmation of Baisden's original work.

By adding the salts in various combinations to a basic medium the authors have shown that the increased growth is mainly due to the zinc; zinc plus copper is better than zinc alone, the effects being almost comparable to those obtained by adding zinc, copper and cobalt. The best results were obtained with either a zinc, calcium, cobalt and copper combination or the complete trace element mixture minus the silver, lead and strontium. Elimination of molybdenum from the zinc, calcium, cobalt, molybdenum, copper, sodium group, decreased the growth, but the further elimination of the sodium restored the growth.

The 3 human strains, PN, DT and C, were used and they gave similar results. In spite of the difference in growth, the total amount of tuberculoprotein produced per litre did not vary greatly and on the deficient medium the yield of protein per gm. of bacilli was greater than on the supplemented media; this may have been due to early moistening of the pellicle with its resultant sinking and autolysis of the bacilli. Glycerol utilization was related to the amount of growth.

As a result of these observations the authors have recommended some modifications to the Dorset synthetic medium and the formula is given in detail.

S. R. M. Bushby

NÉGRE, L., BRETEY, J. & ROY, D. Infra-allergie décelée par les corps bacillaires complets et résistance antituberculeuse conférée par le BCG. [**Infra-Allergy demonstrated by Total Bacterial Cells and Anti-Tuberculous Resistance due to BCG**] *Ann. Inst. Pasteur.* 1958, Sept., v. 95, No. 3, 253–61.

In the 7 experiments described in this paper groups of guineapigs were inoculated with BCG in doses ranging from 0·1 mgm. to 10 mgm. At an interval ranging from 5 to 20 months after inoculation the animals were tested with tuberculin and those failing to react were tested with heat-killed BCG applied intradermally by scarification. The animals were then challenged with living tubercle bacilli, control non-immunized animals being challenged at the same time. In each of the experiments the animals were killed at an interval of 6–9 weeks after challenge.

All the immunized animals showed much less evidence of tuberculosis than did the control animals, irrespective of whether they were still tuberculin-positive, tuberculin-negative but BCG-positive, or had become negative to both antigens. However, in some animals negative to the BCG test, although the protection appeared to be definite, it was less than in those positive to this antigen.

The state of remaining sensitive to the dead BCG after having lost the sensitivity to tuberculin is described as infra-allergy, and the results of these experiments indicate that immunity persists even after this state is lost.

S. R. M. Bushby

TAKAHASHI, Y. & YAMAMOTO, K. Sur les constituants bacillaires déterminant l'allergie et l'immunité dans la tuberculose. [**Bacillary Components determining Allergy and Immunity in Tuberculosis**] *C.R. Soc. Biol.* 1958, v. 152, No. 2, 377–80, 1 fig.

The bacilli from a 35-day-old culture of the Aoyama strain of tubercle bacilli grown in Sauton medium were killed by immersion in acetone and dried; these bacilli were still acid-fast. A portion of the bacilli was alternatively extracted by methanol and chloroform to remove the free lipids; the bacilli were still weakly acid-fast. A portion of the extracted bacilli was further extracted with 1% HCl in alcohol; the bacilli were then amorphous and non-acid-fast.

Doses of equal nitrogen content of the acetone-killed and the 2 extracted bacillary masses were injected intraperitoneally into groups of 7 guineapigs. After 5 weeks the injections were repeated with doses increased 10 times, and 4 weeks later the animals were challenged with viable tubercle bacilli; 6 weeks after the challenge the animals were killed. Tuberculin tests were done each week from the start of the experiment.

The animals immunized with the acetone-killed bacilli showed little evidence of tuberculosis and reacted strongly to the tuberculin, although they became temporarily tuberculin-negative 4 weeks after the 2nd injection of the antigen. The animals immunized with the methanol-chloroform-extracted bacilli showed a little more evidence of tuberculosis but they too reacted strongly to tuberculin. The animals injected with the methanol-chloroform-acid-alcohol antigen showed the same extent of disease as the control unimmunized animals and they did not react to tuberculin until after they were challenged with the living bacilli.

Similar results are claimed in experiments with other strains of tubercle bacilli and thus hypersensitivity to tuberculin and immunity against the tubercle bacillus were obtained with whole bacilli and with bacilli deprived of free lipids but not with bacilli from which the combined lipids have been removed. Thus, immunity and allergy would appear to depend upon the presence of the chemical complex of lipids and protein, with perhaps polysaccharides. *S. R. M. Bushby*

TAKAHASHI, Y. & ONO, K. Réactions d'hémagglutination par les phosphatides du *Mycobacterium tuberculosis*. [**Haemagglutination Reactions by the Phosphatides of** *Mycobacterium tuberculosis*] *C.R. Soc. Biol.* 1958, v. 152, No. 2, 380–83.

In the experiments described in this paper the author shows that red cells coated with phosphatides from the Nakano, Aoyama and BCG strains of the tubercle bacillus are agglutinated by the serum of immunized rabbits and that the antibodies responsible for the reaction are different from those which agglutinate cells sensitized with the tuberculo-polysaccharides. The difference was shown by measuring the agglutination titres of the sera of rabbits injected with living, heat-killed or acetone-killed bacilli, bacilli after extraction with acetone, methanol and chloroform, and bacilli after extraction with acid-alcohol with cells coated with tuberculo-protein, tuberculo-polysaccharide, tuberculo-phosphatides and OT. The separate identities of the antibodies were confirmed by specific neutralization tests. *S. R. M. Bushby*

TAKAHASHI, Y. & HUKAE, H. Étude clinique de la réaction d'hémagglutination par le phosphatide du bacille tuberculeux. [**Clinical Study of the Haemagglutination Reaction with Phosphatide of Tubercle Bacilli**] *C.R. Soc. Biol.* 1958, v. 152, No. 4, 690–92.

In the above paper the agglutination of sheep cells coated with the phosphatide of the tubercle bacillus is shown to be due to antibodies different from those that agglutinate cells coated with the polysaccharides.

The present paper compares the titres of the 2 types of antibodies in 101 sera from persons reacting to tuberculin.

Type of Patients	No.	Antigen	Agglutination Titre 0	2	4	8	16	32	64	128	256	512	1024
Severe tuberculosis	31	Polysaccharide	–	–	–	–	–	1	3	8	8	8	2
		Phosphatide	–	1	–	1	3	6	5	10	4	1	–
Mild tuberculosis	44	Polysaccharide	–	–	1	1	1	3	9	18	9	1	1
		Phosphatide	2	5	2	13	6	8	5	2	1	–	–
Non-tuberculosis	26	Polysaccharide	–	–	–	–	–	3	15	6	1	1	–
		Phosphatide	17	3	3	2	1	–	–	–	–	–	–

In general, although the titres of the antibodies for the phosphatide antigen are lower than those for the polysaccharide antigen, they are relatively higher in those more severely ill and are lowest in the healthy subjects. *S. R. M. Bushby*

SEIBERT, Florence B. **The Interplay of an Immune Substance with Tuberculopolysaccharide and its Antibody in Tuberculosis.** *J. Infect. Dis.* 1958, July–Aug., v. 103, No. 1, 52–60, 1 fig. [25 refs.]

Several publications by the author have suggested that the tuberculo-polysaccharides and their antibodies play an important role in the pathology of tuberculosis [this *Bulletin*, 1957, v. 32, 132, 613; 1958, v. 33, 269]. These papers have shown that animals which produce these antibodies when infected with virulent tubercle bacilli survive longer than those which do not, that the precipitate formed by this antigen and its antibodies is present in caseous material and as the precipitate dissolves in excess antigen, the dissolution may be partly responsible for liquefaction, and that the antigen inhibits complement fixation and causes the disappearance *in vivo* of circulating antibodies.

In the present paper experiments *in vitro* are described which suggest that these polysaccharide antigens block a naturally occurring antituberculous agent of serum and that this effect is abolished by the presence of their specific antibodies. The observations were made on BCG growing as a finely dispersed suspension in Dubos-Middlebrook medium and the effects of the various test agents on the rate of growth of the bacilli were measured turbidimetrically.

Albumin from the serum of tuberculous rabbits was shown to increase growth whereas gamma globulin had the opposite effect. Serum from a rabbit, before and after immunization with BCG, depressed growth and the addition of the tuberculo-polysaccharide to the immune serum increased this inhibitory effect. In general, however, the effects of serum were variable, and the effects of sera which enhanced growth appeared to be related to complement, for heating at 56°C. reduced the stimulation; the net effect of serum appeared, however, to be the balanced effect between the stimulating action of the albumin and the inhibiting action of the gamma globulin.

In experiments in which the gamma globulin from normal rabbits, from rabbits immunized with various tuberculous antigens and from tuberculous ones were compared, the most strongly inhibiting globulins were

shown to be from normal animals and not, as might have been expected, from the immunized animals. The inhibiting factor was therefore not associated with specific antibodies. In further experiments in which the tuberculo-polysaccharide was added with the globulins to the medium the effects in growth were found to vary; with globulins from normal and tuberculous rabbits and from rabbits immunized with either the C protein or the polysaccharide antigen the growth was increased, but with globulins from rabbits immunized with either BCG, A protein or the polysaccharide antigen, growth was inhibited.

These various effects are interpreted as indicating: (1) that tuberculo-polysaccharide inhibits growth only when the serum contains the corresponding antibody and enhances growth when no antibodies or only the anti-tuberculoprotein antibodies are present, and (2) that rather than that antibodies are themselves antimicrobial, certain antibodies can indirectly aid a normally occurring antibacterial substance. This natural antibacterial substance could be lysozyme, especially as there is evidence that its effect on tubercle bacilli depends upon its action on their surface polysaccharides. In experiments in which this enzyme was added to the culture definite inhibition occurred with concentrations of 2 mgm. per 7 ml. and the effect was further increased when gamma globulin was added.

S. R. M. Bushby

Franc, Z., Hais, I. M. & Horsovský, O. **Antituberculous Factors of Milk.** [Correspondence.] *Nature.* 1958, Sept. 27, v. 182, 884–5.

Previous studies have shown that milk contains substances that are active *in vivo* and *in vitro* against tubercle bacilli.

The present paper summarizes attempts to concentrate and characterize the active agents. Milk-whey was adsorbed with charcoal, which retained half the activity and this activity could be eluted with acetic acid. The activity of the dry residue of the eluate was further purified by dissolving it in 90% acetone. The activity could be divided into lipophilic and hydrophilic fractions by partition into an organic solvent. Fatty acids of medium chain-length were identified, among which was lauric acid, but they represented only from 1 to 5% of the activity of this fraction. The more lipophilic fraction was saponifiable with alkali and an active fraction was extracted into bicarbonate from benzene; this fraction contains fatty acid of medium chain-length.

Most of the activity was present with an inhibitor in the hydrophilic fraction and the active component could be adsorbed on to cation exchange column and eluted with 5% ammonia. Further purification was obtained with counter-current distribution between *n*-butanol and acidified water (*p*H 3). Concentrates of the hydrophilic and lipophilic factors which produced 50% inhibition of the growth of H37Rv at dilutions of 1 in 1,000 and 1 in 5,000, respectively produced no inhibition of 5 species of non-mycobacteria at dilutions of 1 in 100, showing that the agents have high antibacterial specificity; however, the concentrates were not active against BCG, *Mycobacterium phlei* or *Myco. smegmatis.*

S. R. M. Bushby

Gancevici, G., Dâmboviceanu, Aristie & Rădulesco, Elena. Recherches sur le facteur inhibiteur de la réaction de Middlebrook-Dubos, isolé du sérum normal de boeuf. [**Studies on the Inhibitory Factor of the Middlebrook-Dubos Reaction, Isolated from Normal Bovine Serum**] *Arch. Roumaines Path. Expér. et Microbiol.* 1957, Dec., v. 16, No. 4, 555–64, 1 fig. & 1 diagram. [21 refs.]

Previous studies have shown that the serum of normal animals contains a factor which inhibits the sensitization of red cells with the soluble antigens of the tubercle bacillus, thus preventing their use in the Middlebrook-Dubos haemagglutination test. This factor is strongest in animals refractory to tuberculosis and it is much reduced in patients with severe pulmonary tuberculosis.

In this paper the isolation of the factor from bovine blood is described. The factor is heat-stable and was isolated from the fluid of the plasma after the plasma had been heated to 100°C. After dialysis and concentration by distillation, the concentrate was freeze-dried and the solid residue extracted with ether in a Soxhlet apparatus for 24 hours. The active factor was further purified by extraction from the residue into acetate buffer *p*H 4·5.

The purified factor contains 65% polypeptide, 31% lipids and 1·85% carbohydrate. It is a white hygroscopic powder, readily soluble in water. It is precipitated by metaphosphoric acid, perchloric acid, trichloracetic acid, ammonium sulphate and uranium acetate.

S. R. M. Bushby

Arima, J., Tsukiori, N. & Takahashi, Y. Sur les changements morphologiques, cytochimiques et biologiques du bacille tuberculeux sous l'influence des chimiothérapeutiques courantes. [**Morphological, Cytochemical and Biological Changes in Tubercle Bacilli exposed to Chemotherapeutic Substances in Current Use**] *C.R. Soc. Biol.* 1958, v. 152, No. 2, 388–91, 3 figs.

H37Rv was grown in Dubos medium for 15 days and then isoniazid, streptomycin and PAS were added to give concentrations of 20 μgm. per ml. After varying periods of further incubation the bacilli were stained by Feulgen's method, Janus green B and toluidine blue for evidence of changes in the nuclei, mitochondria and the meta-phosphatide bodies, and by Zeihl-Neelson stain for changes in acid-fastness. The bacilli were also examined under the electron microscope and tested quantitatively for viability on egg medium.

After 1 day, isoniazid caused an increase in the proportion of non-acid-fast bacilli and a decrease in viability but no changes in the appearance under the electron microscope or in the cytochemical reactions. By 7 days the electron microscope showed an increase in the transparency of the protoplasm, a blurring of the plastides and a diminution of the A bodies, but there were still no changes in the cytochemical reactions. By the 2nd and 3rd week resistant bacilli of normal appearance were present in increasing numbers.

The effects of streptomycin on the electron morphology after 7 days were similar to those of isoniazid, but in addition the number of mitochondria and meta-phosphatide bodies was much reduced although the

nuclei were apparently still unaffected. After 1 day, however, there was a marked reduction in viability and acid-fastness. By the third week resistant bacilli of normal appearance were present.

In contrast to these changes PAS produced little change in the organisms and this is in accordance with the known bacteriostatic action of the drug.

S. R. M. Bushby

KRAAN, J. K. Resistentie van tuberkelbacillen tegen streptomycine, para-aminosalicylzuur en isonicotinezuurhydrazide. [**Resistance of Tubercle Bacilli to Streptomycin, PAS and INH**] *Nederl. Tijdschr. v. Geneesk.* 1958, Nov. 22, v. 102, No. 47, 2314–18.

The English summary appended to the paper is as follows:—

"The problem of the resistance of bacilli to tuberculostatics is becoming increasingly important in the control of tuberculosis everywhere. Of those patients who have already been given tuberculostatic treatment at home, 20–30 per cent. have resistant bacteria, notably to INH, on admission. Of 87 patients admitted in 1952–'53, 34 showed resistance to INH; of 35 patients in 1956–'57, 28 were resistant to one or more tuberculostatics. In most cases resistance was demonstrated on admission, and had nearly always been caused by ineffectual use of tuberculostatics. In most cases only INH had been given.

"Combinations of drugs are important both for a successful therapy and in preventing the development of resistance."

WILLETT, Hilda P. **Inhibition of Diaminopimelic Acid Decarboxylase Activity in** *Mycobacterium tuberculosis* **by Isonicotinic Acid Hydrazide.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 177–9. [11 refs.]

"DAP decarboxylase activity has been detected in cell-free extracts of *Myco. tuberculosis.* Enzyme activity was inhibited by INH and this inhibition could be overcome by pyridoxal phosphate."

NASTA, M., PAUNESCO, E. & GEORGESCO, P. Recherches sur le mécanisme d'atténuation du pouvoir pathogène des variantes isoniazido-résistantes du bacille tuberculeux. [**Studies on the Mechanism of Pathogenicity Attenuation of Isoniazido-Resistant Tubercle Bacillus Variants**] *Ann. Inst. Pasteur.* 1958, Sept., v. 95, No. 3, 272–93, 5 figs. [37 refs.]

This study was made on neutrophil leucocytes from the peritoneal cavity of guineapigs, collected 7–8 hours after the injection of a peptone solution.

In the first experiment suspension of H37Rv and BCG and isoniazid-resistant variants of each were added to the leucocytes and incubated at 37°C.: 120 minutes later 40% of the cells were shown to have phagocytosed bacilli. On an average, the number of bacilli per cell was 5, but rather more of the resistant than of the sensitive bacilli were phagocytosed. The cells containing the bacilli were vacuolated and their nuclei were enlarged and a little indistinct. At this stage staphylococci were added and more were phagocytosed by the cells containing the resistant variants than by those containing the sensitive parent strains; the cells containing the resistant strains were also the more motile and survived the longer.

In the second experiment, in which extracts of the bacilli were added to the neutrophils, the acetone-soluble fraction from BCG was shown to be more toxic than the ether, methanol or ethanol extracts; this fraction from the sensitive strains also had more effect on the motility, viability and depression of phagocytosis of staphylococci than did the same extract from the resistant strain.

In the third experiment the effects of extracts of the bacilli on the bactericidal properties of lysozyme and ribonuclease from the neutrophils from BCG-immunized and unimmunized guineapigs were compared. (The lysozyme was extracted from the cells with saline, and the ribonuclease with acid.) Tuberculin and tuberculo-polysaccharide were found to have a greater effect on the activity of these enzymes from immunized animals, whereas the acetone extract of the bacilli had its greater effect on those from the unimmunized guineapigs.

In the fourth experiment, in which the effects of the acetone extracts of H37Rv and of its isoniazid-resistant variant were compared on these enzymes of an immunized and unimmunized guineapig, the extract from the isoniazid-sensitive organisms reduced the activity more than that from the resistant strain and the reductions were greater with leucocytes from the unimmunized animals than from the immunized animals, especially on the lysozyme activity.

In the last experiment the tubercle bacilli were exposed to the leucocyte extracts for 3 hours and then inoculated into a fluid medium and the growth measured turbidometrically. Exposure to ribonuclease inhibited H37Rv, BCG and both isoniazid-resistant variants to the same degree, there being only slight growth after 11 days' incubation. Exposure to lysozyme had least effect on H37Rv, but on BCG and the isoniazid-resistant bacilli there was a decrease in turbidity, indicating lysis of the organisms.

S. R. M. Bushby

PORTELANCE, V. & FRAPPIER, A. **Some Biological Properties of BCG after the Extraction of Lipids: the Power to Irritate Tissues, the Ability to prepare for and to evoke Bail's Phenomenon, and the Power to sensitize to Tuberculin.** *Canadian J. Microbiol.* Ottawa. 1958, Aug., v. 4, No. 4, 409–20. [15 refs.]

SUTER, E., ULLMAN, Grace E. & HOFFMAN, R. G. **Sensitivity of Mice to Endotoxin after Vaccination with BCG (Bacillus Calmette-Guérin).** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 167–9, 1 fig. [12 refs.]

"1. It is shown that a single intravenous injection of BCG in mice induces a state of hyperreactivity to bacterial endotoxin. The LD_{50} for *E. coli* lipopolysaccharide is decreased from 357 μg in controls to 6 or 7 μg in BCG vaccinated animals. This change

appears around the 5th day after vaccination. 2. Trehalose dimycolate, a component derived from virulent tubercle bacilli induces a similar state of hyperreactivity to endotoxin upon single or repeated injections."

CANETTI, G., BRETEY, J., SAENZ, A., Jr. & GROSSET, J. Effet d'un traitement précoce par l'isoniazide sur l'immunité engendrée chez un cobaye par une dose de BCG standard faible. Données supplémentaires sur le pouvoir vaccinant du BCG isoniazido-résistant. [**Effect of Early Isoniazid Therapy on the Immunity induced in Guineapigs by a Small Dose of Standard BCG. Further Data on the Immunizing Capacity of Isoniazid-Resistant BCG**] *Ann. Inst. Pasteur.* 1958, Sept., v. 95, No. 3, 262–71.

In the first of the experiments described in this paper 30 guineapigs were injected intramuscularly with 10^{-2} mgm. BCG and treated daily for 84 days with 10 mgm. isoniazid subcutaneously. A second group of 24 of the animals were similarly vaccinated but not treated with isoniazid, and a third group of 20 were also untreated but vaccinated with 1 mgm. BCG. A fourth group of 24 guineapigs were vaccinated with 10^{-2} mgm. of a variant of BCG resistant to 25 μgm. isoniazid per ml. 85 days from the day of vaccination the animals were tested with tuberculin and 3 days later challenged with H37Rv; those not dying of intercurrent infections were killed 52 days later. The animals immunized with the small dose of BCG and treated with isoniazid developed only a slight tuberculin reaction and the post-mortem examinations revealed gross tuberculosis, whereas the animals given the same dose of BCG but no treatment developed a strong tuberculin reaction, only slight enlargement of the spleen, and they showed definitely less evidence of tuberculosis than did the treated animals but more than the animals immunized with the larger dose of BCG. The disease in the animals immunized with the isoniazid-resistant BCG was similar to that in the animals immunized with the same dose of the parent strain.

In a second experiment, 2 groups of 35 guineapigs were immunized with 1 mgm. of BCG and 1 mgm. of the isoniazid-resistant variant, respectively, and 42 days later tested with tuberculin. On the 63rd day the animals were challenged with H37Rv and 64 days later the surviving animals were killed. Both groups gave strong tuberculin reactions and both showed much less evidence of tuberculosis than the unimmunized animals challenged at the same time.

This variant of BCG would thus appear to be as antigenic as the parent strain and its use would enable isoniazid therapy and BCG immunization to be practised concurrently. *S. R. M. Bushby*

STEENKEN, W., Jr., SMITH, Marjorie M. & MONTALBINE, V. *In vitro* **and** *in vivo* **Effect of Antimicrobial Agents on Atypical Mycobacteria.** *Amer. Rev. Tuberculosis.* 1958, Sept., v. 78, No. 3, 454–61, 1 fig.

This study was undertaken to determine whether there is a correlation between the *in vitro* and *in vivo* sensitivities of photochromogenic mycobacteria to the antituberculous drugs. The 4 strains examined produced yellow pigment only when exposed to light; they produced good growth at 37°C. in 7–12 days and moderate growth at 33°C. in 16 days; they were neutral-red-negative, catalase-positive and niacin-negative; they were poor cord formers and although they were moderately pathogenic for mice they were avirulent for guineapigs.

The *in vitro* sensitivity of the strains to the antituberculous drugs, against which they were tested *in vivo*, was similar to that of H37Rv except for high resistance to PAS and pyrazinamide. In the *in vivo* tests, mice were infected intravenously with 4 mgm. of the bacilli and groups of 6 were treated with each of the drugs, cycloserine and streptomycin being given by injection and the others in the diet. The strains were not of equal virulence and 100% mortality in the untreated mice was produced by only 1 strain during the experimental period of 31 days (Brownell); with 1 strain (Coffey) there was 100% survival.

Cycloserine, 200 mgm. per kgm. daily, and amithiozone, 500 mgm. per kgm. daily, had little effect on the disease in spite of the bacilli being sensitive *in vitro* to the drugs. Streptomycin, 100 mgm. per kgm. daily, and thiocarbanilide (SU 1906), 500 mgm. per kgm. daily, gave some protection against 2 of the strains (Brownell and Coffey), and isoniazid, 200 mgm. per kgm. daily, and thiocarbanidin (Y 9525), 500 mgm. per kgm. daily, gave good protection against Coffey and Fobes strains and moderate effect against Brownell; against 1 of the strains (Hunt) none of the 6 drugs was effective.

Serial growth in the presence of the drugs showed that the bacilli became resistant to cycloserine, amithiozone, SU 1906 and Y 9525 at about the same rate as does H37Rv, but they became more rapidly resistant to isoniazid and streptomycin. Isoniazid-resistant (100 μgm. per ml.) and streptomycin-resistant (200 μgm. per ml.) variants of Brownell were tested in mice and neither isoniazid nor streptomycin afforded any protection; the isoniazid-resistant variant appeared to be less virulent than the parent strain.

These findings are interpreted as indicating a need for multiple-drug therapy in patients infected with these atypical mycobacteria. *S. R. M. Bushby*

GRABER, C. D., LATTA, Ruth, FAIRCHILD, J. P. & VOGEL, E. H., Jr. **Production of Opalescence by Staphylococci in Egg Yolk Medium, as an Index to Bacteriophage Typability.** *Amer J. Clin. Path.* 1958, Oct., v. 30, No. 4, 314–17, 2 figs.

305 strains of staphylococci from umbilical stumps of 173 infants born in one hospital were tested for coagulase production, ability to split egg yolk and bacteriophage type. Egg yolk tests were performed with freshly isolated strains on 10% egg yolk in Trypticase soy agar.

There was no correlation between coagulase production and ability to split egg yolk. 14 of 24 strains classified as *Staphylococcus aureus* were coagulase negative and split egg yolk. All strains classified on the basis of pigment production as *Staph. albus*, *Staph. citreus* and *Staph. aurantiacus* were egg yolk negative.

76 of 186 coagulase positive strains were egg yolk positive. 74 of these were typable with bacteriophages and 2 produced weak reactions only. 10 strains were egg yolk negative and non-typable.

The phage reactions of the 76 strains are given; only 6 types are represented and 55 strains were typed 52/42B/44/81[= 80]. The egg yolk test is recommended as a screening test to assess the typability of a strain. [These tests were done on very few strains and most of them were representative of the 3 epidemic species in 1 hospital at 1 time. More representative strains must be tested before the egg yolk reaction could be adopted as a reliable screening test for this purpose.] *M. Patricia Jevons*

HURST, Valerie. **Penicillin Resistance of Staphylococci carried by Infants and Young Children.** *J. Lab. & Clin. Med.* 1958, Aug., v. 52, No. 2, 254–8. [11 refs.]

Nose and throat cultures were taken from 208 children aged 15 months to 5 years and from 180 children between 10 and 18 years old, and examined for *Staphylococcus aureus*. The nasal carrier rate rose from 31% in the youngest children to 70% in those aged 10–12, and then fell to 25%. The throat carrier rate was less variable but tended to decrease generally with increasing age. 45% of the children aged 1–5 carried penicillin-resistant staphylococci, compared with 18% of those over 10. Carriage of resistant strains could not be attributed to past treatment with penicillin; it probably arose from infection in the hospital nursery. *R. E. O. Williams*

ROANTREE, R. J., RANTZ, L. A. & HAINES, Elizabeth. **A Medium containing Nucleic Acid, Maltose, and Antibiotics for the Isolation of Group A Hemolytic Streptococci.** *J. Lab. & Clin. Med.* 1958, Sept., v. 52, No. 3, 496–500, 1 fig.

The medium described comprises Difco beef heart infusion agar, 0·6% sodium nucleate, 0·05% maltose, 5% sheep blood, 2 μgm./ml. neomycin and 10 μgm./ml. polymyxin. The nucleic acid was found to increase the diameter and clarity of the haemolytic zone. The antibiotics inhibited the growth of micrococci, *Haemophilus* and *Neisseria*.

In 755 consecutive throat cultures, tested in parallel on the new medium (but containing 5 μgm. neomycin per ml.) and on a simple sheep blood agar, 66 yielded group A streptococci. In 37 cultures there were less than 50 colonies on the control plates, and in 8 of these the new media failed to show any. Of 29 cultures in which 20% or more of the colonies on the control plate were group A streptococci, only 2 might have been misdiagnosed on the new medium. The medium has been used with enthusiasm by a group of paediatricians in practice. *R. E. O. Williams*

GOODER, H. & MAXTED, W. R. **Protoplasts of Group A Beta-Haemolytic Streptococci.** [Correspondence.] *Nature.* 1958, Sept. 20, v. 182, 808–9.

Group A streptococci were incubated with the enzyme derived from a group C phage lysate [this *Bulletin* 1957, v. 32, 1093] in the presence of 2M sucrose or 2M sodium chloride. This enzyme is known to attack the cell wall. Little loss in turbidity resulted from the incubation, but microscopic examination revealed discrete spherical particles. These were thought to be true protoplasts [this *Bulletin*, 1958, v. 33, 972] because they were osmotically sensitive, free from cell-wall antigens, almost free from rhamnose (which occurs almost entirely in the cell wall) and unable to adsorb bacteriophage. They have not been induced to proliferate or to produce new cell wall.

R. E. O. Williams

KRASNER, R. I. & YOUNG, Genevieve. **Role of Hyaluronidase and the Hyaluronic Acid Capsule in the Survival and Dissemination of Group A Streptococci in the Hamster Cheek Pouch.** *J. Bacteriology.* 1958, Oct., v. 76, No. 4, 349–54. [19 refs.]

50 units of hyaluronidase were injected into the cheek pouches of hamsters followed 3 hours later by type 1 and type 4 streptococcal suspensions. More organisms were recovered from surrounding areas on sampling after 6 and 24 hours than from animals which had not been pretreated with hyaluronidase. Petechial haemorrhages were more widespread in the pretreated pouches but lesions in both groups were healed in 12 days. Hyaluronidase alone produced no toxic effects.

Injection of decapsulated streptococci and capsulated organisms resulted in similar lesions although the decapsulated organisms showed a decreased ability to survive in surrounding areas. Organisms from this group recovered from the site of injection after 6 hours were encapsulated and represented the progeny of the decapsulated organisms which had been able to resist phagocytosis. *M. Patricia Jevons*

JELÍNKOVA, Jarmila & JELÍNEK, J. Selektivita bacitracinu ve vztahu k sérologickým skupinám streptokoků. **[Selectivity of Bacitracin in relation to Serological Groups of Streptococci]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 4, 242–51, 7 graphs. [12 refs.] English summary (8 lines).

A statistical analysis has been made of the factors involved in the determination of the sensitivity of haemolytic streptococci to bacitracin by the agar cup method, with the object of developing a reliable test for the identification of strains of group A. The diameter of the zone of inhibition showed a linear regression on the logarithm of agar thickness and the logarithm of antibiotic concentration. The regression coefficient for the latter factor was high (4·1), and to avoid error due to variations in concentration the authors propose the use of the differential coefficient of zone diameter against concentration as a parameter for defining the sensitivity of a strain. The zone diameter also showed a linear regression on the logarithm of the number of colonies; as it is difficult to control this number in practice the authors recommend the use of the regression coefficient (2·17) obtained with a standard strain as a correction factor for computing

the results. The test in the form finally recommended is set up as an 8-point assay with 4 concentrations of bacitracin against a test and a standard strain, the sensitivity of the former being determined in the usual way from the horizontal distance between the 2 regression lines. In the second part of the paper examples are given of the use of the test in practice.

D. J. Bauer

PARNAS, J. & KOZAKOWNA, Regina. Nouvelles recherches sur la variabilité des *Brucella.* [**New Studies on the Variability of** *Brucella*] *Arch. Inst. Pasteur de Tunis.* 1958, June, v. 35, No. 2, 179–97, 9 figs. on 3 pls. [14 refs.]

This is an account of work carried out in the State Medical Institute for Rural Hygiene at Lublin, Poland.

Using the technique of growing brucellae in culture media loaded with disintegrated and dead bacteria closely allied to those inoculated, the authors were able to demonstrate changes both in the biochemical activities of *Brucella* organisms, their sensitivity to thionin and fuchsin, and in their response to monospecific antisera. The dead bacteria used in these observations were killed by exposure to ultrasonic vibration followed by gentle heating.

Such effects were obtained with allied *Brucella* strains and also to a considerable degree when the substrate of dead bacteria was prepared from *Br. tularensis* but not readily if *Escherichia coli* strains were used to provide the substrate of dead bacteria.

A phage acting on *Br. abortus*, which was obtained from the Gamaleia Institute in Moscow, was found valuable in differentiating between *Br. suis* which did not react and *Br. abortus* which did. *Br. abortus* strains, which were modified as above so as to depart from the classical reactions of that strain as defined by HUDDLESON, also failed to react.

J. W. McLeod

RENOUX, G. Comparaison de quelques milieux solides pour la culture des *Brucella.* [**Comparison of Various Solid Media for the Cultivation of** *Brucella*] *Arch. Inst. Pasteur de Tunis.* 1958, June, v. 35, No. 2, 199–210.

A potato extract medium is superior to all others tested and considerably cheaper than the commercial media such as those of Albimi and the tryptose agar of the Difco laboratories. The formula for its preparation is given: 250 gm. finely sliced potato are added to 1,000 ml. distilled water and allowed to infuse at 60°C. overnight. In 1,000 ml. of this extract dissolve by heat Liebig's meat extract 5 gm., NaCl. 5 gm., glycerin 20 ml. and, finally, after adjustment to *p*H 7·0, heat at 150°C. for better solution of components. Check *p*H as 6·8, leave to settle, dissolve 10 gm. Bacto peptone and 25 gm. agar in 1,000 ml. supernatant, sterilize at 121°C. for 35 minutes and add 10% sterile horse serum.

The comparison of the various media depended on results of recovery of strains (42) from the viscera of experimental guineapigs and on counts with 12 strains inoculated directly.

J. W. McLeod

PARNAS, J. & CHODKOWSKI, A., with the assistance of K. LAZUGA & Anna KOZICKA. Experimentelle Untersuchungen über die Immunobiologie der Brucellose und die Wahl der Stämme für einen lebenden Impfstoff für Menschen. [**Investigations on the Immunology of Brucellosis and the Choice of Strains for Living Vaccines for Men**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Oct., v. 116, No. 4, 335–71, 12 figs. [15 refs.]

The English summary appended to the paper is as follows:—

"Immunological, bacteriological and histological examinations were undertaken to study the virulence and antigenicity of Brucella strains: S 19, 45/20, PD, 544, 17, 18, 21, 34 and 42.

"In the first period strain S 19 is very toxic for guinea pigs. Later on it is highly antigenic. Strain 45/20 is completely avirulent and less antigenic. Strain 544 is highly toxic. The toxicity of strain PD, isolated by the authors, is intermediate between 519 and 45/20. This strain has a good antigenicity. It is similar to the USSR strain BA which is used for the production of human vaccines."

STANDFAST, A. F. B. **Some Factors influencing the Virulence for Mice of** *Bordetella pertussis* **by the Intracerebral Route.** *Immunology.* Oxford. 1958, April, v. 1, No. 2, 123–34. [16 refs.]

In order to define the virulence of *Bordetella* [*Haemophilus*] *pertussis* strains for mice, the route of inoculation must be specified since the order of virulence of several strains is different for each of the 3 routes of challenge..

The author finds that toxin plays a part in the intranasal virulence by facilitating the primary lodgement of the organism in the lung, although it does not appear to play any obvious role in intracerebral virulence in which primary lodgement is mechanical. After primary lodgement the ability of the organism to grow in the tissue comes into play and the factors responsible for growth in the lungs and brains do not appear to be identical.

F. T. Perkins

STANDFAST, A. F. B. **The Comparison between Field Trials and Mouse Protection Tests against Intranasal and Intracerebral Challenges with** *Bordetella pertussis.* *Immunology.* Oxford. 1958, April, v. 1, No. 2, 135–43, 2 figs. [11 refs.]

14 vaccines, 10 of which had been tested in the field in the Medical Research Council trials [this *Bulletin*, 1957, v. 32, 228] were assayed in the laboratory for potency in mice challenged by both the intracerebral and intranasal routes. The intracerebral challenge arranged the vaccines in quite a different order of potency from the intranasal challenge. Although reproducible assays can be made by either method field trials have shown that only the mouse potency test with intracerebral challenge corresponds well with protection in the field.

Experiments with 4 of the vaccines were consistent in showing that the antigen responsible for protection against the intracerebral challenge is heat labile, being

destroyed by boiling for 1 hour, whereas the antigen protecting against intranasal challenge is heat stable, losing little of its potency under such conditions.

Comparison of the results with those of FISHER [*ibid.*, 1956, v. 31, 1162] for a particular vaccine K205 [*ibid.*, 1953, v. 28, 1013] shows agreement with the author's work. On the whole, dose response curves of individual intranasal assays are not as consistent as those obtained in intracerebral assays. The author concludes that this may be due to differences in the antigens involved, for 2 different antigens must be responsible, or to differences in the course of infection in the lung and brain. *F. T. Perkins*

DOLBY, Jean M. & STANDFAST, A. F. B. **A Comparison of Passive Protection Tests against Intranasal and Intracerebral Challenges with** *Bordetella pertussis*. *Immunology*. Oxford. 1958, April, v. 1, No. 2, 144–56. [37 refs.]

A survey of a number of rabbit antisera to *Bordetella* [*Haemophilus*] *pertussis* revealed the existence of 2 distinct antibodies, one passively protecting mice against lethal infection by the intracerebral route and the other passively protecting mice against lethal infection by the intranasal route. Neither is the antitoxin. Antisera against most, if not all, S forms of *B. pertussis* contain both types of protective antibody and to a lesser extent to *B. parapertussis* and *B. bronchiseptica*. The authors find that neither of the protective antigens is an agglutinogen or haemagglutinin but they can be distinguished by active protection tests.

Extensive investigations have not led to an *in vitro* test for either of the protective antigens or their antibodies that would replace the mouse test. *F. T. Perkins*

VAINER, Henrietta, FAUR, Yvonne, TIGOIU, Viorica & IONESCU, Honorina. Prepararea unui vaccin *H. pertussis* pe mediu semisintetic solid. [**The preparation of a** *H. pertussis* **Vaccine on a Semi-synthetic Solid Medium**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 123–33. [53 refs.] English summary.

A study has been made of the effect of variations in the composition of the medium upon the growth of 8 strains of phase I *Haemophilus pertussis* used for vaccine production. The medium consisted of 1% of casein hydrolysate, 2·5% gelatin, 0·2% each of starch and charcoal, cystein, tryptophan, yeast autolysate and organic salts. An acid hydrolysate of casein gave better results than enzyme hydrolysates, and growth was not increased by the addition of glycine, cystein or tryptophan. Yeast autolysate was an adequate source of factor V. Haemin and serum albumin were the best sources of factor X, and growth was increased by the addition of sodium sulphite in concentrations of 0·50 and 0·75 mgm. per cc. The results were assessed in all cases by determination of the density of bacterial growth, with microscopical examination and verification of phase I growth. *D. J. Bauer*

FAUR, Yvonne, VAINER, Henrietta, TIGOIU, Viorica & IONESCU, Honorina. Studiul experimental al proprietăților imunizante ale vaccinului *H. pertussis*. [**An Experimental Study of the Immunizing Properties of** *H. pertussis* **Vaccine**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 135–42. [17 refs.] English summary.

An investigation has been made of the immunizing properties in mice of *Haemophilus pertussis* vaccines prepared by various methods. The organisms were grown on the semi-synthetic medium described in the preceding paper, and also on gelatin-blood medium. The degree of immunity produced by vaccination was determined by the survival rate after intranasal infection with an aerosol of *H. pertussis*, and also by serological methods. Vaccines prepared by different methods gave survival rates of 69–82%, compared with 14–22% in unimmunized control groups. An equal degree of protection was obtained with vaccines prepared on the 2 media, whereas 8–13% greater protection was obtained with vaccines inactivated with formaldehyde at room temperature instead of 37°C. No difference was observed between the agglutinin titres and protection indices of the sera of rabbits and mice immunized with vaccines prepared on the 2 different media. *D. J. Bauer*

POZSGI, N., FAUR, Yvonne & TIGOIU, Viorica. Studiul experimental al componenței *H. pertussis* din trivaccinul diftero-tetano-pertusis. [**An Experimental Study on the** *H. pertussis* **Constituent of Diphtheria-Tetanus-***H. pertussis* **Triple vaccine**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 143–9. [31 refs.]

An investigation has been made of the effects of mixture with diphtheria and tetanus toxoids upon the immunogenicity of *Haemophilus pertussis* vaccine, and was carried out by the parallel immunization of groups of mice with triple vaccine absorbed on aluminium phosphate, Hungarian triple vaccine of a similar type, unabsorbed triple vaccine and *H. pertussis* vaccine, followed by challenge with a virulent strain of *H. pertussis* by intracerebral inoculation or by inhalation of aerosol. In all cases the LD50 of the *H. pertussis* component was of the same order (2×10^8–3×10^8 organisms), and a similar range of agglutinin titres was found in the surviving animals. The results thus show that the immunogenicity of the *H. pertussis* component was not affected by the presence of diphtheria and tetanus toxoids. *D. J. Bauer*

LIN, Tong-Ming. **Studies on** *pertussis* **Vaccine. II. Comparative Studies on the Potency of Plain** *pertussis* **Vaccine and the** *pertussis* **Component in DTP Vaccine.** *J. Formosan Med. Ass.* 1958, Mar., v. 57, No. 3, 141–4.

The mouse protection test, with intracerebral challenge, was used to assay the potency of the pertussis component of a diphtheria-tetanus-pertussis vaccine in which alum-precipitated toxoids were used. In the same test the potency of the pertussis vaccine alone was assayed. In 5 tests, each involving 1 of 5

pairs of different vaccines, the potency of the pertussis component of the combined vaccine was always slightly higher than that of the pertussis vaccine alone. The differences, however, are so small that unless several repeat tests were done they may be statistically insignificant. *F. T. Perkins*

ANDERSEN, Else K. & BENTZON, M. W. **Comparison between Pertussis Vaccine Potency Assays in Mice challenged by the Intracerebral Route and Mice challenged by the Intranasal Route (Sublethal Dose).** *Acta Path. et Microb. Scandinavica.* 1958, v. 42, No. 4, 333–56, 5 figs. [18 refs.]

The potencies of several pertussis vaccines were assayed by means of the mouse protection test, in which the mice were challenged intracerebrally in one series and intranasally with a sublethal dose in another.

It was found that when the same virulent strain of *Haemophilus pertussis* was used for both intracerebral and intranasal challenge the results of potency assays were very similar. With the intranasal challenge test the protective potency of a vaccine was independent of both the ability of the challenge strain to induce lung oedema and of the variations of infecting doses used. When different and freshly isolated strains were used for intranasal challenge the variation in potency of the same vaccine was unusually high and this was taken by the authors as a suggestion of difference in antigenic composition of the freshly isolated strains.

F. T. Perkins

HORIO, T., HIGASHI, T., NAKAI, M., KUSAI, K. & OKUNUKI, K. **Preparation of Crystalline *Pseudomonas* Cytochrome$_{551}$ from *Pseudomonas aeruginosa*.** [Correspondence.] *Nature.* 1958, Nov. 8, v. 182, 1307–8, 2 figs.

WATSON, R. G.; SCHERP, H. W.; MARINETTI, G. V. **The Specific Hapten of Group C (Group II α) Meningococcus. I. Preparation and Immunological Behavior** [WATSON & SCHERP] *J. Immunology.* 1958, Oct., v. 81, No. 4, 331–6. [20 refs.] **II. Chemical Nature** [WATSON, MARINETTI & SCHERP]. *Ibid.*, 337–44, 2 figs. [17 refs.]

i. "Soluble specific substances were prepared from 3 representative strains of Group C (formerly Group II α) meningococci. Dilutions as high as 1 : 4,000,000 of all preparations gave positive precipitin reactions with homologous rabbit antiserum. However, all evidenced some degradation of immunologic integrity, *e.g.*, the best preparation absorbed only $\frac{3}{4}$ of the homologous mouse-protective activity from a rabbit Group C antiserum and it failed to engender significant active immunity in mice. On the other hand, intraabdominal injection of 30 μg of this preparation/animal sharply diminished the immune response of mice to subsequent injections of an effective Group C vaccine. The precipitin reactions of these substances with an equine polyvalent antimeningococcal serum prepared in 1918 indicated that Group C meningococci had been isolated in the United States at that time, although they were not recognized as a distinct group until 1940."

ii. "The specific hapten of Group C (formerly Group II α) meningococcus appears to be predominantly a polymer of a sialic acid congener, as evidenced by its nearly complete conversion to humin-like material on aqueous acid hydrolysis, specific colorimetric analyses, infrared absorption spectrum, periodate oxidation, quantitative elementary and group analyses, correlation of sialic acid content with serologic activity, and conversion by hydrolysis in methanolic hydrochloric acid into products having characteristics of a sialic acid. Hexosamine determinations and nitrogen content indicate that this polymer contains hexosamine units as well as sialic acid units."

THOMPSON, R. E. M. & KNUDSEN, A. **A Reliable Fermentation Medium for *Neisseria gonorrhoeae*: A Comparative Study.** *J. Path. & Bact.* 1958, Oct., v. 76, No. 2, 501–4.

Identification of the gonococcus depends ultimately on demonstration of its ability to ferment glucose but not maltose. 2 types of fermentation media were tested—(1) a solid medium consisting of peptone, sodium chloride, agar (25 gm. per litre), tryptic digest broth and distilled water with added phenol red; (2) similar to (1) but agar only 0·15%. (3) agar 0·15%, phenol red and peptone-water to 100%. (4) agar 0·15%, phenol red, Hartley's tryptic digest broth to 100%.

The main difference between the 2 types is that (1) is solid and (2) (3) and (4) are "sloppy".

With 55 strains of gonococci results showed that satisfactory results were obtained with medium (1) in 70%, medium (2) in 84%, medium (3) in 58% and medium (4) in 98%.

The key to the problem seems to be a low agar content, while Hartley's digest broth, rich in amino acids, with 5% rabbit serum gave prolific growth.

T. E. Osmond

RANQUE, J., SENEZ, J. C. & DEPIEDS, R. Essais sur la survie de *Treponema pallidum* (souche Nichols). [**Trials on the survival of *Treponema pallidum* (Nichols strain).**] *C.R. Soc. Biol.* 1957, v. 151, No. 7, 1407–9.

Prolonged survival of spirochaetes is necessary for certain tests; the method of NELSON and MAYER is satisfactory and well-known. The present authors have obtained good results by using human or animal sera; a 5% extract of embryonic mice and 10% of human or sheep serum in physiological solution works well provided the spirochaetes are kept in an atmosphere of 95% nitrogen and 5% CO_2.

As an alternative method they employed 0·3 cc. of a reducing agent with 1 cc. of spirochaete suspension in rabbit serum in a hermetically sealed tube; survival was very poor; when placed in an atmosphere of nitrogen and 5% CO_2 results were very favourable; when the atmosphere was of nitrogen without CO_2 survival was poor. It seemed therefore that anaerobiasis alone was not sufficient but that CO_2 also was necessary.

In a further experiment the tubes were placed in an anaerobic jar emptied of air and containing 4% CO_2; results were better but not very good. They then tried

a third method which consisted in placing the material in a sterile test tube with a cotton wool bacteriological filter inserted to a point 2 cm. above the suspension with a second absorbent wool plug soaked in saturated carbonate of soda and an equal quantity of 40% watery solution of pyrogallol; the tube was then closed with an indiarubber cork. It was found that if 0·5 cc. of pyrogallol and 0·5 cc. of carbonate of soda were used and if the cork was sealed with paraffin the survival of spirochaetes was satisfactory *i.e.* 72%–96%.

It is concluded that reducing agents are not toxic and that anaerobiasis and the presence of CO_2 are both essential for the survival of spirochaetes.

T. E. Osmond

LILLY, H. A. **A Study in Culture Methods for Clostridia.** *J. Med. Lab. Technol.* 1958, July, v. 15, No. 3, 165–74, 2 figs. on 2 pls. [26 refs.]

Attention is drawn to the value of media containing neomycin for the isolation of *Cl. welchii* from material in which it is present in mixture with other bacteria.

Neomycin added to Nagler plates in the concentration of 100 μgm./ml. facilitates the direct isolation of type A *Cl. welchii* and even better results are obtained by preliminary cultivation in Robertson's chopped meat broth followed by subculture to neomycin Nagler agar plates.

It was found that when 112 samples of faeces were examined by direct plating on Nagler agar 17 positive results were obtained of which 9 were false positives, *i.e.* due to colonies other than *Cl. welchii* which developed lecithinase, whereas on the neomycin Nagler plate 70 positives were observed which were all due to *Cl. welchii*.

On the same material incubated for enrichment in the cooked meat broth and subcultured to Nagler agar, 57 were found to give positive colonies of which 13 were "false" whereas subculture to the neomycin Nagler agar gave 89 true Nagler reactions.

For *Cl. welchii* of the types B, C, D and E, however, a lower concentration of neomycin *i.e.* 50 μgm./ml. is recommended—a level at which other bacteria were still inhibited. Solutions of neomycin [10,000 μgm. per ml.] and agar plates in which neomycin was incorporated remained active for long periods if kept at + 2°C.

J. W. McLeod

SEKI, T., TAKAKI, M., OKAMURA, G. & SAKAGUCHI, A. **Tetanal Toxin obtained by Mechanical Disintegration of the Bacterial Cell.** *Med. J. Osaka Univ.* 1958, Mar., v. 8, No. 4, 639–51, 10 figs.

It is possible to demonstrate the presence of toxin in the cell content of young cultures of *Clostridium tetani* disintegrated by sonic vibration or by grinding after careful preliminary washing. The MLD lags behind the Lf value in the first 5 minutes and at 30 minutes or beyond. This is attributed to liberation of protoxin in the early stages and of formation of toxoid later. At 10 minutes Lf and MLD correspond. Differential centrifugation shows that very little toxin is associated with the cell wall or with any particulate matter spun down at 30,000 r.p.m. It remains in the supernatant.

J. W. McLeod

DOLMAN, C. E. **Recent Observations on Type E Botulism.** *Canadian J. Pub. Health.* 1957, May, v. 48, No. 5, 187–98, 4 figs. [16 refs.]

The number of type E strains of *Clostridium botulinum* now known is considered as well over 100. Dr. Dolman has collected some 50 strains and subjected them to detailed study of their distinctive cultural, biochemical and toxigenic properties. The paper is a detailed and most valuable account of type E. The various laboratory tests used are set out. With glucose peptone beef infusion broth the toxic strains show very distinctive effects, including vigorous gas formation without proteolysis which may continue for several days. These toxigenic strains tend to become atoxic because they readily degenerate into an opaque and sporulating (OS) colonial mutant, or less often into a transparent and proteolytic mutant (TP). These mutants, whether cultivated alone or together, are incapable of toxin production, but either of them may revert to the toxic phase.

All *Clostridium botulinum* cultures, regardless of their type, have a well-known tendency to become non-toxigenic. Type E strains seem particularly prone to become atoxic.

An interesting account is also given of various mutations in these atoxic strains, particularly of some from Russian sources. These include variations in phase type, some being OS–TP mixture while the remainder studied were wholly in the OS phase. All toxic cultures apparently tend to degrade to a sporulating atoxic (OS) phase, but the rate and extent of the degradation vary widely. The studies on the activation of type E strains are particularly interesting. Type E toxins can be activated by incubation for a few hours at 37°C. with 1% trypsin at about *p*H 6 so that their mouse lethalities may increase up to 10,000-fold or more. Preliminary tests suggest that the antitoxin-binding power of such activated toxins is not markedly affected.

A special note is included on the outbreaks which have taken place in Labrador and Alaska and on other outbreaks in adjacent parts of the world.

The author remarks that in nature type E strains presumably occur in the OS phase and being non-toxic, they may be overlooked in routine soil or food surveys and even in the examination of suspected foodstuffs.

The size of the problem is indicated by the author's statement that to date 32 type E outbreaks have been recorded, involving a total of 145 persons with 56 deaths, *i.e.* a case fatality of 38·6%.

W. G. Savage

CARACÒ, A., FALCONE, G. & SALVATORE, G. Sull'azione di alcuni aminoacidi sulla germinazione da L-alanina di spore di *B. subtilis.* [**Action of some Amino-Acids on the Germination by L-Alanine of the Spores of** *Bacillus subtilis*] *Giorn. di Microbiol.* Naples. 1958, Mar.–Apr., v. 5, No. 2, 127–36, 3 figs. [17 refs.] English summary.

STRANGE, R. E. & THORNE, C. B. **Further Purification Studies on the Protective Antigen of *Bacillus anthracis* produced *in vitro*.** *J. Bacteriology.* 1958, Aug., v. 76, No. 2, 192–202, 7 figs. [12 refs.]

Culture filtrates of *B. anthracis* have been processed with a view to obtaining a highly purified and concentrated antigen for the purpose of immunization. A filtrate of the cultures was treated by fractional ammonium sulphate precipitation and the greater part of the activity located in that part of the precipitate at 50% saturation which, after solution in Tris buffer and adjustment to *p*H 5·0, remained in solution. This was further purified by absorption on alumina and elution with 0·1 M phosphate buffer. The fraction so obtained appeared to be homogeneous both by the criteria of movement in an electrophoretic field and sedimentation in the ultracentrifuge. This purified antigen reacted in gel diffusion plates with a single sharp and continuous line equally with rabbit sera immunized with the homologous material and with horse sera prepared with injection of spores of *B. anthracis* at Porton. The content of the solution prepared was reckoned as 5,000 units per ml. taking as a unit the amount required to give a just perceptible line of reaction in the gel diffusion plates. Injected in 5 equal doses containing a total of 2·5 μgm. it afforded active immunity to rabbits so that most of those injected could resist 250 lethal doses of spores. The antigenic protein described appears to be very liable to degradation if the period of culture is prolonged and this degradation is attributed, in all probability, to the action of a digestive enzyme of the nature of peptidase which is thrown out of action if the reaction is alkaline, *i.e.* *p*H 8·0–9·0. *J. W. McLeod*

FUNGI

LARSH, H. W., SCHOLES, V. E., HINTON, Agnes & SILBERG, S. **Minimal Infectious Inoculum of *Histoplasma capsulatum* for Mouse and Chick Embryo.** *Proc. Soc. Exper. Biol. & Med.* 1958, July, v. 98, No. 3, 570–73.

Infection of mice can be induced by the inoculation of a single macroconidium of *Histoplasma capsulatum* (AJELLO and RUNYON, *Pub. Health Monograph*, No. 39, 1952). To determine the frequency of success with minimal inocula of mycelial phase cultures of *H. capsulatum* the present authors used single germinated and non-germinated macroconidia and microconidia and non-branched hyphal fragments selected by means of a Chambers micromanipulator.

Inocula derived from 3-month-old cultures and suspended in broth containing streptomycin and penicillin were given intraperitoneally to Swiss white mice, and inocula from 3-month-old and 3-year-old cultures were injected into the yolk sac of 5-day-old white Leghorn chick embryos. Full details of the technique employed are given.

Liver, spleen and adrenals of mice which died after 3 days or were killed after 8 weeks were cultured. Chick embryos which died after 3 days were triturated and cultured, and in those surviving 18 days the liver, spleen and adrenals were cultured.

Infection of mice resulted from each type of spore inoculum but not from the hyphal fragment. 5% of 182 mice were infected and the non-germinated macroconidium was the most successful agent. Of 571 chick embryos approximately 8% were infected. The highest rate was obtained with the hyphal particle in both 3-month and 3-year cultures, but infection resulted from all types of inocula except the non-germinated macroconidium in the case of the 3-month culture. *Jacqueline Walker*

DI MENNA, M. E. ***Candida albicans* from Grass Leaves.** [Correspondence.] *Nature.* 1958, May 3, v. 181, 1287–8.

The author writes from the Soil Bureau, Wellington, New Zealand, to say that he has found *Candida albicans* 3 times in a sample of grass. This is the third report of the recovery of this organism from a vegetable source, and it seems probable that it commonly occurs on vegetation. But since up to 50% of normal people carry it in the intestinal tract, exposure to it must be a daily experience, and there is no public health problem. *Charles Wilcocks*

TOMSÍKOVÁ, Alena & WAGNER, V. Inkomplette Antikörper bei der *Candida*-Gruppe. [**Incomplete Antibodies against the *Candida* Group**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Sept., v. 116, No. 3, 239–45, 3 graphs. [41 refs.]

SOLOTOROVSKY, M., QUABECK, G. & WINSTEN, S. **Antifungal Activity of Candidin, Nystatin, Eulicin, and Stilbamidine against Experimental Infections in the Mouse.** *Antibiotics & Chemotherapy.* New York. 1958, July, v. 8, No. 7, 364–71. [30 refs.]

In a comparative study of the *in vivo* effect of candidin, nystatin, eulicin and stilbamidine on mice experimentally infected with *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Candida albicans* and *Cryptococcus neoformans*, the authors found candidin to be the most effective of the 4 against *H. capsulatum* and *C. albicans* and eulicin the most effective against *B. dermatitidis* and *C. neoformans*. Neither of these antibiotics, however, was as well tolerated as nystatin, which as expected, was active against *H. capsulatum*, *C. albicans* and *C. neoformans*. Stilbamidine had little effect against any of the infections except those of *B. dermatitidis*. *Jacqueline Walker*

GADEBUSCH, H. H. **Active Immunization against *Cryptococcus neoformans*.** *J. Infect. Dis.* 1958, May–June, v. 102, No. 3, 219–26. [20 refs.]

"A number of possible immunizing antigens were prepared from whole Cryptococcus cells and from cells decapsulated by acid hydrolysis employing grinding, freeze-thawing or supersonic oscillation. Only ground whole cells were capable of stimulating protective antibody formation. Products of sonic treatment of

whole cells and grinding of decapsulated cells appeared to have a toxic effect on mice.

"Crude polysaccharides isolated from various strains of cryptococci did not protect mice against a lethal challenge dose of homologous organism either alone or in combination with an ion exchange resin adjuvant.

"Purified polysaccharides, on the other hand, elicited a minimal protective response which was markedly increased by the addition of the same adjuvant.

"Purified polysaccharides when injected in high doses were shown to be capable of inducing 'immunological paralysis' in mice.

"Resin-polysaccharide-tracer studies have shown the polysaccharide to be eluted in small amounts in vivo.

"The probable mechanism of action of the ion exchange resin and of all preparations has been discussed."

GADEBUSCH, H. H. **Passive Immunization against** *Cryptococcus neoformans*. *Proc. Soc. Exper. Biol. & Med.* 1958, July, v. 98, No. 3, 611–14.

Protection of mice for a limited period against lethal doses of a number of strains of *Cryptococcus neoformans* was achieved by passive immunization with corresponding absorbed hyperimmune rabbit sera. The homologous monovalent serum gave the longest protection, but the disease developed eventually in all the mice when the injections of antiserum were stopped.

With mouse polymorphonuclear leucocytes and small- and large-capsuled cells of a strain of *C. neoformans* it was shown that phagocytosis occurred frequently both *in vivo* and *in vitro* with the small-capsuled cells but only rarely in the case of those with large capsules.

It is suggested that the limited protection by the antiserum may possibly be due to the presence of ablastins or other non-absorbable humoral factors acquired as a result of immunization.

Jacqueline Walker

RICKETTSIAE

WEYER, F. Beobachtungen bei der Übertragung von brasilianischem Fleckfieber und sibirischem Zeckenbissfieber auf die Kleiderlaus. [**Notes on the Transmission of Brazilian Typhus and Siberian Tick-Bite Fever in the Body-Louse**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1958, v. 9, No. 3, 174–93, 10 figs. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 291.]

ZUBKOVA, R. I. **Survival of** *Rickettsia burneti* **in Milk and Milk Products.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1259–63. [24 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 292.]

BREZINA, R. **Contribution to the Study of Phase Variation in** *Coxiella burneti*. *Acta Virologica*. Prague. 1958, Apr.–June, v. No. 2, 91–102, 7 figs. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 292.]

BACTERIOPHAGES

VALERIU, A. Recherches sur l'origine et le mécanisme du maintien du bactériophage dans le milieu extérieur. [**Investigation into the Mechanism of Survival of Bacteriophage in an External Medium**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, July–Aug., v. 6, No. 5, 419–40, 6 figs. [42 refs.]

In an attempt to elucidate the mechanism of the survival of bacteriophage the author studied the ecology of 3 different sources: the intestine of those suffering from enteric infections, septic tank liquor and naturally polluted water. The bacterial content and the relative number of lysogenic bacteria were estimated in each case. It was found that a high proportion of the bacteria present in each case were lysogenic. It was also observed that certain latent phages could be transformed into active lytic phages capable of multiplying on homologous and heterologous strains. The possibility that certain lytic phages can also multiply under external conditions on related heterologous strains is put forward. *E. Windle Taylor*

KANTOCH, M. Własności serologiczne bakteriofagów anty-Vi pałeczki durowej. [**Serological Properties of Anti-Vi Phages of Typhoid Bacilli**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1957, v. 5, 129–65, 2 figs. [27 refs.] English summary.

A study has been made of certain serological relationships of anti-Vi phages of *Salmonella typhi*.

The A, D, E and F phages were not neutralized by antisera to the homologous organisms over a period of 24 hours. A considerable degree of antigenic relationship between the phages was found in cross-neutralization tests with phage antisera which had been absorbed to remove bacterial antibodies. The phage neutralization test was carried out in parallel with the Widal test on sera from 120 patients suffering from typhoid. Both tests were positive in 17 instances (14·2%), the neutralization test was positive and the Widal test was negative in 19 (15·8%), the neutralization test was negative and the Widal test positive in 22 (18·2%), and both tests were negative in 62 (51·8%). In a similar examination of sera from control groups of healthy persons or patients suffering from other infectious diseases phage antibodies were found in only 3·8% of 210 instances. Phage neutralizing antibody usually did not appear until after the 10th day of illness, and the method would therefore not be of great value in diagnosis. *D. J. Bauer*

MAYR-HARTING, Anna. Die Entwicklung von Phagenlöchern und der Mechanismus der Phagenwirkung in festen Nährböden. [**Development of Phage Plaques and the Mechanism of Phage Action in Solid Media**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 171, Nos. 6/7, 380–92, 7 figs. [16 refs.]

A study has been made of the rate of development of phage plaques, with a phage of *Escherichia coli* which produces plaques up to 12 mm. in diameter. The plaques became visible after incubation for 2–3 hours, and their diameter increased arithmetically for 15–20 hours and then remained constant. The diameter of the plaques was unaffected by pre-incubation of the host organisms for 6–24 hours, or by proximity of the plaques to each other, but was somewhat reduced by decreasing the thickness of the agar layer, and greatly reduced by increasing the density of the bacterial suspension. *D. J. Bauer*

TOMIZAWA, J. **Sensitivity of Phage Precursor Nucleic Acid, synthesized in the Presence of Chloramphenicol, to Ultraviolet Irradiation.** *Virology.* New York. 1958, Aug., v. 6, No. 1, 55–80, 6 figs. [27 refs.]

The author has shown that UV-irradiation of bacteria containing phage precursor DNA leads to the production of uninfective phage particles. This was demonstrated by stopping protein synthesis with chloramphenicol and allowing DNA to accumulate, then irradiating *Escherichia coli* B cells labelled with ^{32}P and infected with T2. After irradiation, chloramphenicol was removed and the production of phage particles allowed to continue. Although DNA synthesis continued, as estimated by ^{32}P content, more than half of the phage which accumulated was uninfective. With higher doses of UV it was found that the irradiated culture never resumed synthesis of DNA at the normal rate, that complete phage particles were formed more slowly than in unirradiated cultures, and that although the phage particles produced were normal with regard to P content, optical density and bacterial killing power, none were infective.

Experiments with ^{32}P showed that DNA synthesized in the presence of chloramphenicol was efficiently incorporated into phage particles after removal of the inhibitor, whether or not the infected cells were irradiated. The number of uninfective particles produced was proportional to the amount of phage precursor irradiated, indicating that UV light had a direct action on phage precursor DNA. It was possible that the phage particles were uninfective either (a) because they contained DNA damaged genetically by UV irradiation, or (b) because a final step in DNA synthesis had been blocked by the effect of irradiation. The evidence favoured hypothesis (a), as phage whose precursor DNA had received a given dose of UV light and normal infective phage receiving an equal dose showed the same efficiency in multiplicity reactivation and marker rescue experiments.

It was found that phage which was uninfective because its DNA contained lesions caused by irradiation of precursor DNA nevertheless contained no more of the irradiated DNA than infective particles released at the same time. It seemed that in the assembly of the phage particles irradiated and unirradiated precursor DNA were mixed, but the identity of the fractions was preserved. Thus the precursor DNA which was sensitive to genetic damage by UV irradiation already possessed specific molecular organization equivalent to that contained in the finished phage particle.

J. Taverne

BERTANI, G. & SIX, E. **Inheritance of Prophage P2 in Bacterial Crosses.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 357–81, 1 fig. [23 refs.]

"Prophage *P2* may be located on the genetic chromosome of the host cell (*Escherichia coli* strain *C*) by crossing genetically marked lysogenic strains. At lysogenization, prophage *P2* establishes itself at a specific locus (location I or preferred location). In the process of double lysogenization by means of superinfection of a singly lysogenic strain, the second prophage establishes itself at a different locus. Two such second-choice locations are recognized. In superinfection of doubly lysogenic strains, substitution of the prophage in location I occurs more often than substitution of the prophage in the second-choice location. A temperate phage closely related to *P2*, but belonging to a different immunity class, behaves like *P2* in respect to location choice.

"In doubly lysogenic strains the prophage in the preferred location contributes more heavily than the other prophages to the phage yield of the lysogenic cells."

RAETTIG, H. & DRESCHER, J. Adsorptionsvorgänge bei Virusarten. III. Mitteilung: Untersuchungen über die Reaktion von T_3-Phagen mit spezifischen Antikörpern. [**Adsorption in Different Types of Virus. III. The Reaction of T_3 Phages with Specific Antibodies**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 171, Nos. 6/7, 393–400, 2 figs. [10 refs.]

A study has been made of the amount of T3 phage neutralized by serial dilutions of specific antiserum and the results obtained could be shown to be consistent with the Freundlich adsorption isotherm, in that the logarithm of the amount of phage neutralized divided by the antibody concentration had a linear regression on the logarithm of the amount of phage remaining after neutralization. It was possible to use this relationship to determine the antibody content of an antiserum in relation to a standard preparation.

D. J. Bauer

EPSTEIN, R. H. **A Study of Multiplicity-Reactivation in the Bacteriophage T4. I. Genetic and Functional Analysis of T4D.–K12 (λ) Complexes.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 382–404, 7 figs. [26 refs.]

"An investigation of multiplicity reactivation (MR) in the bacteriophage T4 has revealed new information regarding the reactivation process. Restitution of a complete genetic structure occurs in a mating of parental structures. It appears that no multiplication of genetic structures occurs prior to the formation of

this genome. Evidence is presented which suggests that the ultraviolet (UV) damages stimulate recombination in the neighbourhood of their locations in the genetic structure. Some of the UV damage affecting critical viral functions is shown to be localized in the genetic structure of the phage. Still another effect of the damage is shown to be associated with unspecified functions not necessarily required for the reactivation of the genome. These two effects of UV appear to form a relatively large proportion of the sensitive target in MR."

VIRUSES

In this section the abstracts are arranged as far as possible in the following order:—General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

SMITH, W. **Virus-Host Cell Interactions.** [Leeuwenhoek Lecture.] *Proc. Roy. Soc.* Ser. B. 1958, Mar. 18, v. 148, No. 932, 370–84. [24 refs.]

The stages of entry of the virus, multiplication and release from the cell of the progeny are discussed on the basis of the events occurring in the T-phages, and a comparison is drawn between attachment of phage and red cell agglutination by influenza virus. The author casts doubt upon the view that the virus enzyme is required for cell penetration and subsequent multiplication, since it has been shown that poorly eluting particles still retain their infectivity, and he suggests that the specific attachment of virus to cell is brought about by other groupings insusceptible to enzyme action. Elution could then afford a second opportunity of bringing about an attachment which was not successful immediately. The concept of the eclipse phase comes in for some criticism, and symbiosis and the nature of viruses are also discussed.

D. J. Bauer

MARCUS, P. I. & PUCK, T. T. **Host-Cell Interaction of Animal Viruses. I. Titration of Cell-Killing by Viruses.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 405–23, 5 figs. [30 refs.]

"Destruction of mammalian cell reproductive capacity by virus was quantitatively measured by attaching Newcastle disease virus (NDV) to monodisperse HeLa cells up to a multiplicity of 5 and scoring the fraction of survivors as colony counts after 8–10 days' incubation. Single-cell survival experiments in this range of attached virus demonstrate that a single particle of NDV is sufficient to kill a HeLa cell.

"Microscopic examination of individual HeLa cells, 95% of which have received a killing particle of NDV, reveal no significant difference from uninfected cells in the fraction which attach, and spread on glass 5–15 hours after seeding. However, such infected cells do not undergo even one reproductive division.

"NDV plaque-forming-particle (PFP) and hemagglutinating-particle (HAP) survival curves for ultraviolet radiation and heating to 55° are presented. Exposure of NDV to specific antiserum, heating to 55°, or ultraviolet radiation results in loss of its ability to kill host cells.

"This technique permits titration of single virus particles which can produce recognizable changes in single cells without requiring successive waves of infection.

"Aspects of the cell-killing actions of NDV and T2 bacteriophage are discussed."

FERRIS, R. D. & PLOWRIGHT, W. **Simplified Methods for the Production of Monolayers of Testis Cells from Domestic Animals, and for the Serial Examination of Monolayer Cultures.** *J. Path & Bact.* 1958, Apr., v. 75, No. 2, 313–18, 6 figs. on 2 pls. [10 refs.]

The authors describe in detail a method for obtaining monolayer cultures of testis cells from pigs and calves. The cells are released by the action of 0·25% trypsin, and after filtration through a double layer of muslin and centrifugation for 5 minutes at 1,000–1,200 r.p.m. the cells are suspended in growth medium to give 1–1½ million cells per ml. The growth medium consists of Hanks saline with 0·5% lactalbumin and 0·1% yeast extract and 5–10% of ox serum. After a growth period of 48–72 hours a similar medium made up in Earle saline is substituted. The appearance of the cultures, showing both polygonal epithelial type cells and also fibroblast-like cells, is illustrated. The stained cultures were prepared on coverslips and grown in Petri dishes which were contained in a specially built Perspex box which fitted into a standard bacteriological incubator. The box is fitted with slide valves so that it can be flushed out with 5% CO_2 in air. The *p*H of the cultures can be observed through the Perspex and the preparation regassed as necessary. The authors point out that this tissue from domestic animals is readily obtainable as many of these are castrated as a routine. They note that the cells have proved useful for the study of rinderpest, vaccinia and an unidentified agent isolated from a calf's kidney.

A. J. Beale

HEYMANN, H., GULICK, Z. R., DE BOER, C. J., DE STEVENS, G. & MAYER, R. L. **The Inhibition of Ribonuclease by Acidic Polymers and their Use as possible Antiviral Agents.** *Arch. Biochemistry.* 1958, Feb., v. 73, No. 2, 366–83. [36 refs.]

A number of acidic polymers have been investigated as possible inhibitors of ribonuclease, and an attempt has been made to correlate inhibitory activity with antiviral activity. The inhibitory effect was investigated by adding a solution of the compound under test to a solution of sodium ribonucleate at *p*H 5·0; ribonuclease was then added, and the enzyme activity was determined from the amount of phosphorus soluble in trichloroacetic acid-uranyl acetate reagent liberated after incubation for 10 minutes. A similar determination was made in the absence of the test compound, and the

degree of inhibition was given by the ratio of the 2 values. Antiviral activity was investigated in fertile eggs infected with 100 ID50 of the PR8 strain of influenza virus or with 50 LD50 of vaccinia virus; absence or reduction in titre of influenza haemagglutinin after 24 hours' incubation and prolongation of survival time by 3 days in eggs infected with vaccinia were taken as criteria of antiviral activity. 66 polymers were studied, and the results obtained are presented in a table. A number of compounds showed high anti-ribonuclease activity; 17 compounds were active against influenza and 27 against vaccinia, and all these compounds were ribonuclease inhibitors.

D. J. Bauer

RHODES, A. J. & VAN ROOYEN, C. E. **Textbook of Virology for Students and Practitioners of Medicine.**

[This book was reviewed on p. 182.]

KUBELKA, V., SLAVÍK, K. & SOUSEK, O. Ein Beitrag zum Studium der Hepatitis infectiosa. (Vorläufige Mitteilung.) [**A Contribution to the Study of Infective Hepatitis (Preliminary Communication)**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 171, Nos. 6/7, 401–12, 7 figs. [10 refs.]

From the mixed sera of 2 patients suffering from infective hepatitis an infective agent was obtained by inoculation of the allantoic cavity of chick embryos and subsequent transfer from the allantoic fluid to monkey kidney tissue cultures. The agent produced a cytopathogenic effect with rounded cells and syncytia, progressing to complete destruction of the cultures. It was also pathogenic for young mice, which died with lesions in the liver 5–7 days after intraperitoneal infection with culture fluid. By appropriate procedures the infection in mice was shown to be unconnected with ectromelia or *Eperythrozoon coccoides*. In tissue culture neutralization tests antibody to the agent was found in the sera of patients suffering from infective hepatitis. A skin test antigen prepared from formalin-inactivated culture fluid gave a positive reaction in 57% of 200 patients with hepatitis and in 31·6% of 60 control subjects. By means of filtration through collodion membranes the particle size of the agent was estimated as 100–200 mμ. *D. J. Bauer*

HOLT, S. J. & EPSTEIN, M. A. **Cytochemical and Electron Microscopical Observations on Substances associated with Fluorocarbon Purified Vaccinia Virus.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 472–9, 10 figs. (8 coloured) on 2 pls. [Numerous refs.]

This paper reports the findings of chemical and cytochemical investigations of ultracentrifugates of fluorocarbon-purified vaccina virus. The authors concentrated their attention on the jelly associated with the virus. It was found to consist of deoxyribonucleic acid associated with a polysaccharide. Centrifugates from normal chorio-allantoic membranes similarly prepared and studied contained polysaccharide but no DNA. The DNA was not dissolved from unfixed smears by prolonged treatment with cold distilled water; this suggests that it was either highly polymerized or present as nucleoprotein. The authors hold the opinion that the DNA is derived from host cells rather than from virus. [This must, of course, be true at some level of argument, but the absence of DNA in the absence of virus infection does suggest that the origin of this material may have a closer connexion with the virus than the authors appear to think. It would be interesting to know the relationship between this material and the nucleoprotein antigen of vaccinia virus described by SMADEL, RIVERS and HOAGLAND (this *Bulletin*, 1943, v. 18, 254).] *Colin Kaplan*

ZEITLENOK, N. A., PILLE, E. R. & KONOSH, O. V. **Effect of Dyes on Virus Haemagglutination.** *Problems of Virology*. London. 1957, v. 2, Nos. 5/6, 282–7. [Translated from Russian.]

Because acridine compounds have been shown to inhibit the multiplication of vaccinia virus, the authors decided to investigate the interactions of these substances with virus and host cells *in vitro*. The system chosen was the vaccinia haemagglutination reaction. They found that amino-acridines agglutinated red cells and that there was a relationship between haemagglutination and inhibition of vaccinia virus. By varying both vaccinia haemagglutinin dilution and dye concentration they were able to show that some of their compounds (notably mepacrine) also inhibited haemagglutination. This inhibition was shown to be due to the action of the mepacrine on the red cells. After treatment with mepacrine red cells were unable to adsorb haemagglutinin. Other dyes tested did not have this effect. Mepacrine was also shown to be able to reverse, almost completely, agglutination which had already taken place. None of the dyes tested (including mepacrine) had any effect on influenza virus haemagglutination. [Since vaccinia haemagglutination is related, not to the virus particle, but to a separable haemagglutinin which contributes nothing to the infectivity of the virus, the point of this study seems to be somewhat blunted.] *Colin Kaplan*

BAUER, D. J. **The Chemotherapeutic Activity of Compounds of Copper, Rhodium and certain other Metals in Mice infected with Neurovaccinia and Ectromelia Viruses.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 480–89, 4 figs.

An assay technique based on the linear relationship between virus dose and reciprocal survival time was developed and applied to the study of the chemotherapeutic activity of metal compounds on neurovaccinia and ectromelia infections in mice. All of 5 different cupric compounds were shown to have a chemotherapeutic activity in vaccinia infections. Cuprous chloride was without effect. Of 45 other elements investigated, rhodium, indium and platinum were the only ones to show chemotherapeutic activity in neurovaccinia. Copper, rhodium, zinc and, to a less extent, platinum were effective against ectromelia but indium had no effect on this infection. The 2 infections differ, therefore, in their response to indium and

zinc compounds. None of the compounds studied had any action on 23 additional viruses causing neurotropic infections in mice. Possible mechanisms of the chemotherapeutic action of the metal compounds are discussed.

H. G. Pereira

BEDSON, S. P. & GOSTLING, J. V. T. **Further Observations on the Mode of Multiplication of Herpes Virus.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 502–9. [10 refs.]

The early stages of multiplication of herpes simplex virus in chick embryo cell suspensions was investigated. Under the experimental conditions employed it was demonstrated that approximately 2% of the cells were initially infected with an average of 1 pock-forming unit per cell. After 4 hours' incubation only one-tenth of the virus initially presented could be detected in culture homogenates obtained by different methods, including disruption by shaking with ballotini on a Mickle machine. No similar drop of infective titre could be detected, however, when titrations were made on culture materials with whole cells. These findings suggest that the residual virus detected in homogenates prepared at 4 hours' incubation does not take part in the process of virus multiplication. The low infectivity of culture homogenates at the early stage of the growth curve may be due to (a) an essential and very intimate virus-cell linkage, or (b) virus breakdown into non-infective sub-units.

H. G. Pereira

GROSSGEBAUER, K. Dunkelfeld- und phasenkontrastmikroskopische Beobachtungen in Verbindung mit serologischen Untersuchungen an Myxoviren. **[Dark Field and Phase Contrast Microscopic Observations in connexion with Serological Investigations on Myxoviruses]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 171, Nos. 6/7, 430–49, 9 figs. on pl. [51 refs.]

A description is given of the morphology of filamentous forms of 17 strains of influenza and related viruses. Cross-agglutination tests were carried out with filament preparations of all the strains and their respective antisera. Agglutination with homologous antiserum was observed in most cases, but there was a considerable degree of cross-reaction and the method was not suitable for the purpose of strain identification.

D. J. Bauer

VERSTEEG, J., MOUTON, R. P. & VERLINDE, J. D. Aziatische influenza bij paarden? **[Asian Influenza in Horses?]** *Tijdschr. v. Diergeneesk.* 1958, July 15, v. 83, No. 14, 608–13. English summary.

An investigation has been made of the incidence of antibodies to a locally isolated strain of Asian influenza virus in 124 pig and 79 horse sera collected in the Netherlands during the autumn of 1957 at the time of the epidemic. Inhibiting antibody was not present in the pig sera, but was present in titres up to 48 in 21 horse sera; neutralizing antibody was present in 4 of 6 sera examined by means of intranasal neutralization tests in mice. A horse infected intratracheally with Asian influenza virus grown in mouse lung produced inhibiting antibody in a titre of 48 and neutralizing antibody in a titre of 160 2 weeks after infection.

D. J. Bauer

CHESBRO, W. R. & HADRICK, L. R. **Comparison of the Tendency to cling to Glass and Haemagglutination produced in Erythrocyte Suspensions by Ferric Chloride and by Influenza Virus.** [Correspondence.] *Nature.* 1958, Oct. 25, v. 182, 1164, 1 fig.

The mechanism of virus haemagglutination was studied by comparing the tendency of red cells to cling to glass beads after treatment by influenza virus or by a colloid suspension of ferric chloride. The results suggest that haemagglutination is due, not to the formation of virus "bridges", but to the hydrophobic character of the virus-erythrocyte complexes which tend to aggregate and to cling to glass (shield formation) under the influence of surface tension [this *Bulletin*, 1958, v. 33, 187].

H. G. Pereira

LENNETTE, E. H., CULVER, J. O. & STEVENS, Thirza E. **The Type-Specific Reactivity of the Influenza Complement Fixation Test. Inability of Allantoic Fluid Antigens to Distinguish between Asian and other Recent Type A Influenza Virus Infections.** *J. Lab. & Clin. Med.* 1958, Oct., v. 52, No. 4, 605–11, 1 fig. [15 refs.]

Acute and convalescent sera collected over a period of years from patients with influenza were tested by haemagglutination inhibition and complement fixation against A-prime and Asian influenza viruses. The antigens used for complement fixation consisted of unprocessed allantoic fluids from infected chick embryos. Antibody responses to infections by A-prime or Asian influenza viruses could be distinguished by haemagglutination inhibition but not by complement fixation. It is suggested that the type-specificity of the complement-fixation test is due to the soluble (S) antigen which overshadows the strain-specific reactivity of the viral (V) antigen [see also HENLE *et al.*, this *Bulletin*, 1958, v. 33, 710]. Advantages for the use of type-specific complement-fixation tests for diagnostic purposes are discussed.

H. G. Pereira

ISAACS, A., BURKE, D. C. & FADEEVA, Lydia. **Effect of Interferon on the Growth of Viruses on the Chick Chorion.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 447–51.

Inoculation of UV-irradiated influenza virus or of interferon on the dropped chorio-allantoic membrane of embryonated eggs was shown to inhibit the multiplication of influenza virus subsequently added to pieces of the same membrane *in vitro*. Interference was localized to the dropped portion of the membrane. These findings were applied for the study of the effect of interferon on the multiplication of vaccinia, cowpox, ectromelia and herpes simplex viruses in the chick chorio-allantoic membrane. Multiplication of vaccinia virus was greatly inhibited by interferon, as shown both by pock counts and by haemagglutinin titrations.

Comparable results were obtained with cowpox and ectromelia viruses. Interferon had no demonstrable effect on the multiplication of herpes simplex.

H. G. Pereira

BURKE, D. C. & ISAACS, A. **Some Factors affecting the Production of Interferon.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 452–8.

The authors investigated the production of interferon in pieces of chick chorio-allantoic membrane inoculated with influenza A virus preparations inactivated by different methods. Good interferon yields were obtained with virus preparations inactivated by UV irradiation or by heat. With lightly irradiated virus preparations, interferon production was shown to proceed for 3 days following inoculation. Formalin-inactivated virus or incomplete virus prepared by serial passages of undiluted infective allantoic fluids gave rise to very little or no interferon production. The ability of different types of virus preparations to induce interference and to produce interferon were, in general, correlated. No interferon production was observed during the first 24 hours after inoculation of live virus, but at later periods interferon accumulated in the cultures. However, pre-treatment with heat-inactivated virus conditioned the membrane to produce interferon within the first 24 hours after addition of live virus. It is suggested that, after incubation with heated virus, the synthetic ability of the cells is directed towards the production of interferon rather than that of virus.

Interferon production in chick chorio-allantoic membranes was also obtained by the use of irradiated influenza B, fowl plague and Newcastle disease viruses. Low yields of interferon were obtained in cultures of monkey kidney or HeLa cells inoculated with irradiated influenza A virus. *H. G. Pereira*

ISAACS, A. & BURKE, D. C. **Mode of Action of Interferon.** *Nature.* 1958, Oct. 18, v. 182, 1073–4.

Production of interferon after the inoculation of live influenza virus on to chick chorio-allantoic membranes pre-treated with heat-inactivated virus has been previously demonstrated [Burke and Isaacs, above]. In the present report it is shown that interferon production can also be stimulated by live virus in membranes pre-treated with interferon. Possible explanations for the mode of action of interferon are discussed. It is suggested that the synthetic mechanism of interferon-treated cells is conditioned to the production of more interferon and that this mechanism can be stimulated by viral ribonucleic acid.

H. G. Pereira

STAKHANOVA, V. M. **Non-Specific Influenza Virus Inhibitors in the Sera of Pyrexial Patients.** *Problems of Virology.* London. 1957, v. 2, Nos. 5/6, 373–7, 3 figs. [Translated from Russian.]

Non-specific inhibitors of influenza virus haemagglutination were found to appear and to reach high titres in the sera from rabbits with artificial pyrexia induced by subcutaneous injections of turpentine. Thermolabile (beta) inhibitors appeared earlier and reached higher titres than thermostable (alpha) inhibitors. The levels of inhibitor titres varied directly with severity of inflammation. Both inhibitors were destroyed by treating the sera with CO_2. Tests for non-specific inhibitors were also carried out in acute and convalescent sera from patients with a variety of pyrexial conditions and revealed higher inhibitor titres in acute than in convalescent sera. It is concluded that removal of non-specific inhibitors is essential for the diagnosis of influenza by the haemagglutination-inhibition test. *H. G. Pereira*

BORECKÝ, L., with the technical assistance of L. MAASOVÁ & J. KIANICKOVÁ, J. **A Factor destroying Virus Receptors in Pneumococcal Cultures. I. Isolation and Properties of the Factor.** *Acta Virologica.* Prague. 1958, Apr.–June, v. 2, No. 2, 73–83, 2 figs. [17 refs.]

A factor with properties similar to those of receptor-destroying enzyme has been found in cultures of pneumococci, and has been designated Pn-f-103. After incubation with a filtrate of a culture of type I pneumococcus (strain 103) for 2 hours at 37° chick red cells were unable to absorb the PR8 and Lee strains of influenza virus. The cells also became agglutinable by a number of different animal sera. The factor appeared in the cultures after 2 days of incubation, and the highest titres were attained when the organisms were grown in veal broth with 10% rabbit serum; it did not cause haemolysis, was insensitive to decalcifying agents and was inactivated by trypsin.

D. J. Bauer

AMOS, H. & VOLLMAYER, Elizabeth. **Inhibition of Influenza Virus Synthesis by 2-Thiouracil.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 337–47. [16 refs.]

Inhibition of multiplication of influenza virus (PR8) by 2-thiouracil was studied in de-embryonated eggs and in cultures of minced chorio-allantoic membrane. Thiouracil in concentrations varying from 20 to 200 μgm. per ml. caused a marked reduction in haemagglutinin production. This effect was observed when thiouracil was added up to 16 hours after the virus inoculum, while its addition at 24 hours did not affect the yield. The inhibitory action of thiouracil was counteracted by uracil. Incorporation of ^{32}P and ^{14}C-guanine into RNA of infected or uninfected membranes was inhibited by thiouracil. These results suggest that the inhibitory action of thiouracil may be due to interference with RNA synthesis. Virus yields from membranes incubated with low concentrations of thiouracil had relatively low infectivity titres, suggesting production of incomplete virus. *H. G. Pereira*

CARSON, H. G. **The Comparative Susceptibility of Various Tissue Culture Cell Lines to Adenovirus Types 1–7.** *J. Med. Lab. Technol.* 1958, Oct., v. 15, No. 4, 257–60.

Adenovirus types 1 to 7 were titrated in cultures of a variety of cell types, including 2 human cell lines

(HeLa and amnion strain FL) and trypsinized human amnion, and human, monkey, rabbit, calf and guinea-pig kidney. The susceptibility of the different cells to adenoviruses was estimated from titration end-points based on cytopathic effect read at 4 days' incubation. HeLa cells were found to be the most susceptible and their use for the cultivation of adenovirus types 1 to 7 is recommended. *H. G. Pereira*

ROWE, W. P., HARTLEY, Janet W., ROIZMAN, B. & LEVY, H. B. **Characterization of a Factor formed in the Course of Adenovirus Infection of Tissue Cultures causing Detachment of Cells from Glass.** *J. Exper. Med.* 1958, Nov. 1, v. 108, No. 5, 713–29. [22 refs.]

"Infectious tissue culture fluids of the majority of serotypes of adenovirus at low dilutions detach HeLa or KB cells from glass surfaces within a few hours after inoculation. A reproducible method for testing cell detachment was devised.

"The factor present in infectious tissue culture fluids and responsible for cell detachment is trypsin-sensitive and non-dialyzable; it is smaller and more resistant to the effect of heat or ultraviolet light than the infectious virus particle.

"Cell detachment activity was found to be temperature-dependent, and the cell-detaching titer of infectious tissue culture fluids was not affected by repeated exposure to HeLa cells. Inhibition of cell detachment by human or rabbit sera was observed only when other antibodies to adenovirus antigens were also present, but the antibody inhibiting cell detachment could not be correlated quantitatively with complement-fixing or homologous neutralizing antibody."

DEINHARDT, F., MAY, R. D., CALHOUN, H. H. & SULLIVAN, H. E. **The Isolation of Adenovirus Type 1 from a Fatal Case of Viral "Pneumonitis".** *Arch. Intern. Med.* 1958, Nov., v. 102, No. 5, 816–19. [17 refs.]

FUKUMI, H., NISHIKAWA, F., MIZUTANI, H., NAKAMURA, K., WATANABE, T., KITAYAMA, T. & KINOSHITA, T. **A Cytopathogenic Agent isolated from a Case of an Upper Respiratory Illness resembling an Adenovirus Infection.** *Japanese J. Med. Sci. & Biol.* 1957, Dec., v. 10, No. 6, 397–406, 6 figs. on 2 pls. [13 refs.]

A cytopathic agent (named 67-57 virus) was isolated from a child with febrile pharyngitis and conjunctivitis by inoculation of throat swab material into HeLa cell cultures. The cytopathic effect caused by this agent was similar to that of enteroviruses. Differentiation of the 67-57 virus from myxoviruses, Coxsackie viruses, polioviruses and adenoviruses was established by serological tests. It was also distinguished from croup-associated (CA) virus, herpes simplex and JH-2060 viruses by host-range and type of cytopathic effect. No serological comparison with ECHO viruses could be made for lack of standard antisera. Acute and convalescent sera from the patient showed a 16-fold rise in neutralizing antibody for the 67-57 virus and no antibody rises for influenza A and B, adenovirus and streptococcus MG. Neutralizing antibody for the 67-57 virus was found in 16 of 26 sera from young adults and in 19 of 32 sera from infants aged 2–3 years. *H. G. Pereira*

MARSTON, R. Q. **Cytopathogenic Effects of Hemadsorption Virus Type 1.** *Proc. Soc. Exper. Biol. & Med.* 1958, Aug.–Sept., v. 98, No. 4, 853–6, 3 figs.

The cytopathic effect of type 1 haemadsorption virus [CHANOCK *et al.*, this *Bulletin*, 1958, v. 33, 621] in HeLa cell cultures was studied by phase-contrast cinemicrography and by examination of stained cultures. Early changes, occurring approximately 12 hours after inoculation, consisted of coalescence of the cytoplasm of adjacent cells resulting in giant cells containing hundreds of nuclei. The central area of the lesions was subsequently detached from the glass, leaving characteristic holes in the cell sheet. No morphological alterations in nuclei or mitochondria could be detected until distortion of the whole cell sheet made further study difficult or impossible. No nuclear division in the absence of cytoplasmic division was ever observed. *H. G. Pereira*

VOGEL, F. S. **Enhanced Susceptibility of Proliferating Endothelium to Salivary Gland Virus under naturally occurring and Experimental Conditions.** *Amer. J. Path.* 1958, Nov.–Dec., v. 34, No. 6, 1069–79, 5 figs. on 2 pls. [11 refs.]

"A 10-year-old boy with a fatal disseminated salivary gland virus infection showed characteristic cytomegaly with intranuclear and intracytoplasmic inclusions in the salivary gland, heart, lung, liver, pancreas, adrenals, kidney, esophagus, gastrointestinal tract, central nervous system, smooth and skeletal muscle, and conspicuously in the endothelium and mesothelium of a chronic proliferative peritonitis.

"The presence of cytomegaly and intranuclear inclusions in the proliferating endothelial cells of the peritoneum and their absence elsewhere in non-proliferating endothelium suggested that these cells have increased susceptibility to the salivary gland virus during maturation. Experimental studies made it clear that proliferating endothelial cells of the blood vessels in sand granulomas of mice have a notably greater susceptibility to the mouse strain of salivary gland virus than does nonproliferating endothelium elsewhere in the same animal. The findings broaden previous observations on the effect of cellular state upon the susceptibility to viruses."

DARNELL, J. E., Jr. & EAGLE, H. **Glucose and Glutamine in Poliovirus Production by HeLa Cells.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 556–66, 3 figs. [19 refs.]

In earlier work EAGLE and HABEL [this *Bulletin*, 1956, v. 31, 1270] showed that HeLa cells produce poliovirus as well in a medium containing only glucose, glutamine

and balanced salts as in more complex media. This paper is an expansion of this work, confirming this finding. The yield of poliovirus per cell was greatly decreased in Earle balanced salt solution compared with that in a complete growth medium for HeLa cells. The inadequacy of salt solution was more clearly shown if the HeLa cells were first starved for 6 hours in salt solution before infection. The addition of glucose (5 mM) and glutamine (2 mM) to salt solution raised the yield to that obtained in complete medium. However, starved cells produced roughly half the yield of poliovirus per cell. Glucose alone added to salt solution only achieved 20–30% of the maximal yield. Fructose could substitute for glucose, though 10–20 mM solutions were required. Galactose, ribose, pyruvate, ribose and pyruvate, and ribose 5-phosphate were inadequate as substitutes for glucose. Glutamic acid (10–20 mM) substituted for glutamine for virus production. With a strain of HeLa cells adapted to grow on 2 mM glutamic acid it was found that 5 mM glutamine or 1 mM glutamic acid now produced a similar increase in virus yield. The effect of added glutamine is presumably to replace the glutamine which disappears rapidly from the amino-acid pool when HeLa cells are starved. *A. J. Beale*

BASSET, J. & MAURIN, J. Les effets des hautes pressions sur les virus. Variations avec la température de la pression d'inactivation du virus de la poliomyélite en culture de tissus. [**The Action of High Pressures on Viruses. Influence of Temperature on the Inactivating Pressure of Poliovirus in Tissue Culture**] *Ann. Inst. Pasteur.* 1958, Oct., v. 95, No. 4, 374–84, 3 figs.

The effect of high pressure on poliovirus Type 2 was investigated in infected monkey kidney tissue culture fluid. Virus was subjected to an increased pressure in special rubber sacs. It was found that inactivation was effected at a lower pressure and more quickly at + 2–4°C. than at 37°C. The pressure required to reduce the titre by one-half (a difference which is not easy to determine accurately with the dilution assay technique used) in 30 minutes was estimated as 6,650 (kgm./cm.^{2}) at + 2°C. and 7,825 (kgm./cm.^{2}) at 37°C. *A. J. Beale*

POHJANPELTO, P. **Stabilization of Poliovirus by Cystine.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 472–87, 9 figs.

Incubation of a heat-sensitive strain (t+) of poliovirus with L cystine greatly reduces the sensitivity to temperatures less than 50°C. The effect takes 6 hours at 37°C. to become maximal. A concentration of 50 μgm. per ml. produced the greatest effect. The effect is specific for L cystine and is probably due to the combination of the L cystine with SH groups in the protein forming cross links which resist the uncoiling effect of heat. The effect of L cystine is prevented by *p*-chloromercuricbenzoate and reversed by thioglycollate. The t+ strain of virus contains heat stable particles but these particles are not rendered heat sensitive by prior thioglycollate treatment. Anaerobic conditions also render the virus much more stable to heat. *A. J. Beale*

TAYLOR, Joyce & GRAHAM, A. F. **Purification of Poliovirus labeled with Radiophosphorus.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 488–98, 1 fig. [22 refs.]

Type 2 poliovirus (MEF 1 strain) was labelled with ^{32}P by propagating the virus in monkey kidney cells in the presence of ^{32}P. The non-viral ^{32}P was removed by dialysis and adsorption of the virus and subsequent elution from an ion exchange resin. Dowex-1 anion exchange resin (250–500 mesh, 10% cross-linked) was used. Virus was passed through the column at 2·25 ml. an hour (this slow flow rate was essential for quantitative adsorption and the technical method used to achieve it is described). Virus was eluted in a single peak together with the ^{32}P by 0·05M NaCl. The resulting viral eluate was purified again by 1 cycle of ultracentrifugation. This step removed most of the remaining ^{32}P not associated with the RNA component of virus. The ^{32}P of this purified virus behaved in the ultracentrifuge in the same fashion as the infectious poliovirus particle. *A. J. Beale*

LEDINKO, Nada. **Production of Noninfectious Complement-Fixing Poliovirus Particles in HeLa Cells treated with Proflavine.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 512–24, 1 fig. [18 refs.]

Proflavine has been found to interfere with the production of T2 phage by *Escherichia coli.* The bacteria are still lysed but non-infective phage material is released [this *Bulletin*, 1956, v. 31, 73]. This paper describes somewhat similar observations on the poliovirus-HeLa system. It was found that the addition of proflavine to HeLa cells suppressed the yield of infectious poliovirus. Some effect was noted with 0·02 μgm. per ml. but the maximum effect was with 2·5 μgm. per ml. Proflavine inhibited the production and release of intracellular poliovirus within 30 minutes of its addition to cells, at any stage in the growth cycle. The effect was on the cells, not on the virus. Maximal effects were noted when the proflavine was used 1–5 hours before virus addition or during the latent phase. If cells to which proflavine had been added 1–5 hours previously were washed and infected, inhibition was still noted, but if the cells were incubated for a few hours at 37°C. before virus infection the effect of proflavine was greatly reduced. Monkey kidney cells (second generation) and an FL strain of human amnion cells behaved in the same manner. Although no infective virus was released from proflavine-treated cells, the cells degenerated in exactly the same manner as normal virus-infected cells. Also the cells produced the same quantity of poliovirus complement-fixing antigen as untreated cells. The number of physical particles looking like poliovirus was also similar in proflavine-treated and normal cells. Normally the ratio

of physical particles to plaque forming units was $3{\cdot}7 \times 10^2$ for these HeLa cells, and in the presence of proflavine it was $1{\cdot}3 \times 10^6$. *A. J. Beale*

KELLY, Sally & SANDERSON, W. W. **The Effect of Chlorine in Water on Enteric Viruses.** *Amer. J. Pub. Health.* 1958, Oct., v. 48, No. 10, 1323–34, 5 figs. [12 refs.]

The inactivation of enteroviruses by chlorine was investigated by using partially purified viruses and water rendered free from chlorine demand. It was found that the usual conditions for the disinfection of water supplies were inadequate to kill enteric viruses completely. Thus a concentration of free residual chlorine of 0·2–0·3 p.p.m. at *p*H 7 required a contact period of at least 30 minutes to give complete inactivation. Different virus strains were inactivated at markedly different rates. 2 recently isolated Type 1 polioviruses were inactivated at a much slower rate than the stock Mahoney Type 1 strain; Coxsackie B1 virus and poliovirus Type 3 Saukett strain were inactivated at the same rate as the newly isolated Type 1 poliovirus. On the other hand the Mahoney strain of Type 1 poliovirus and Coxsackie B5 virus were inactivated considerably more quickly. It was thought possible that the variations in sensitivity to chlorine of different strains of virus might be due to the presence of some resistant particles in strains that had not been passed frequently in tissue culture. The effects of *p*H level, concentration of residual chlorine and temperature on the time required to kill 99·7% of the virus strains were estimated. A rise in *p*H above 6 caused a delay in inactivation time which was much more noticeable at 4°C. than at room temperature and with the more slowly inactivated virus strains. It is concluded that for the inactivation of enteric viruses in water *p*H 7 at 25°C. requires a minimum free residual chlorine concentration of 0·3 p.p.m. acting for at least 30 minutes. At higher *p*H levels or lower temperatures more intensive chlorination is required.

A. J. Beale

BÖTTIGER, Margareta, LYCKE, E., MELÉN, B. & WRANGE, G. **Inactivation of Poliomyelitis Virus by Formaldehyde. Incubation Time in Tissue Culture of Formalin treated Virus.** *Arch. f. d. gesamte Virusforschung.* 1958, v. 8, No. 2, 259–66, 2 figs. [10 refs.]

Poliovirus when treated with formaldehyde requires a longer time than untreated virus for the production of cytopathic effects in tissue cultures [see this *Bulletin*, 1958, v. 33, 1190]. This paper furnishes additional experiments demonstrating this fact. Thus for untreated virus there is very little difference in titre when tubes are read after 7 or 14 days' incubation, although there may be a slight increase (about 0·3 log. unit) between 4 and 7 days. By contrast, virus treated with formaldehyde for 3 days shows a progressive increase in titre with time of incubation amounting to 1 log. unit in titre between 4 and 14 days. The same phenomenon is noted when the plaque assay method is used although the plaques, once they have appeared, grow at the same rate as those due to untreated virus.

A. J. Beale

DARNELL, J. E., Jr., LOCKART, R. Z., Jr. & SAWYER, T. K. **The Effect of Neutral Red on Plaque Formation in Two Virus-Cell Systems.** [Correspondence.] *Virology.* New York. 1958, Oct., v. 6, No. 2, 567–8.

In the plaque technique for virus assay neutral red is used as the stain to differentiate areas of living and dead cells. The stain is either incorporated in the nutrient agar overlay or added after a period of 48–72 hours has elapsed for virus growth. Experiments are described which show that the number of plaques of poliovirus grown on HeLa cells or western equine encephalitis virus grown on chick fibroblasts is almost halved if the stain is incorporated in the agar rather than added later to demonstrate already formed plaques. The effect appears to be due to the action of neutral red on the cells. It is not due to an effect on virus adsorption. It occurs in 2 virus cell systems employing different nutrient media. Experiments are reported to be under way to determine whether it occurs when the host cells have been purified by clone isolation. *A. J. Beale*

PARKS, J. J., GANAWAY, J. R. & PRICE, W. H. **Studies on Immunologic Overlap among Certain Arthropod-Borne Viruses. III. A Laboratory Analysis of Three Strains of West Nile Virus which have been studied in Human Cancer Patients.** *Amer. J. Hyg.* 1958, Sept., v. 68, No. 2, 106–19. [31 refs.]

This is an attempt to compare the virulence and immunogenic potential of low-passage Egypt 101 (Strain 5), high-passage West Nile strain 1, and the tissue-culture-passaged strain Lennette-Koprowski of West Nile virus. Various monkeys were infected but only *Ateles* spp. were found to be satisfactory for tests of viraemia after subcutaneous inoculation. In these Egypt 101 was more virulent than Lennette-Koprowski as judged by viraemia. Intracerebral inoculation of cynomolgus and rhesus monkeys showed that the most severe symptoms were caused by Egypt 101; Lennette-Koprowski was found to cause severe histological evidence of encephalitis. When the strains were inoculated into chicks 6–14 days old, Egypt 101 caused higher and more prolonged viraemia. Neutralizing antibodies were found to have the same titre against all 3 strains. Egypt 101 caused higher titres of both homologous and heterologous antibody probably because it multiplies best. When formalin-killed Egypt 101 and West Nile strain 1 were compared for antibody production in mice and chicks, no differences in antigen make-up were apparent. Chicks previously infected with West Nile had marked protection against circulation of Japanese encephalitis virus. The authors conclude that none of the 3 strains is suitable for human live vaccines.

[See also this *Bulletin*, 1958, v. 33, 804.]

C. E. Gordon Smith

WINN, J. F., KAPLAN, W., PALMER, D. F. & SOLOMON, G. **Sensitivity of Swine and Cattle to Artificial Infection with Western Equine Encephalitis Virus.** *J. Amer. Vet. Med. Ass.* 1958, Nov. 1, v. 133, No. 9, 464–6.

"Cattle and swine were experimentally inoculated with various doses of Western equine encephalomyelitis virus (WEE). The cattle did not develop detectable virus even though doses in the range of 34,000,000 chick $l.d._{50}$ were given. The cattle subsequently developed neutralizing antibodies although, in 2 of the 4 heifers, the indexes were very low.

"Swine seem to have a threshold of infection of about 42,000 chick $l.d._{50}$. Virus was recovered from the blood of infected swine at 1 : 10 dilutions, and neutralizing indexes from 200 to 15,900 resulted three weeks after inoculation. These species are not suitable for sentinel animals and probably do not constitute a reservoir for WEE virus."

KEEBLE, S. A., CHRISTOFINIS, G. J. & WOOD, W. **Natural Virus-B Infection in Rhesus Monkeys.** *J. Path. & Bact.* 1958, July, v. 76, No. 1, 189–99, 7 figs. on 2 pls.

The authors describe a small outbreak of ulcers on the lips and tongues of a group of 18 rhesus monkeys just arrived from India. 6 of the 18 were affected and subsequent examination of 1,400 monkeys revealed 32 cases. 2 of 66 in one batch had lesions on arrival. The monkeys examined were aged 1–2½ years and cases were predominantly in the younger animals. Ulcers were commonest on the tongue; situated on the dorsum they were initially vesicular, then broke down, forming yellowish-grey plaques. The monkeys did not appear to be inconvenienced by them. Virus was most easily isolated from the vesicle fluid. Lip lesions were usually at the muco-cutaneous junction and followed a similar but shorter course than those on the tongue. There was 1 shoulder lesion, probably due to a bite. The histology of the lesions is described and illustrated. Histological changes were found in the pons and medulla and around the roots of the trigeminal or facial nerves. Inflammatory changes were observed in the liver and kidneys. Virus isolations were made in monkey kidney-cell monolayers and their identity was confirmed by rabbit passage and neutralization tests.

Rabbits inoculated either intradermally or on the cornea died in 5–7 days of encephalomyelitis affecting particularly the medulla and cervical cord. Keratitis developed in 3–5 days after corneal inoculation. Inoculation of a monkey in the thalamus failed to produce infection of the nervous system, while 2 other monkeys inoculated peripherally showed local lesions and 1 had histological changes in the central nervous system similar to those found in natural infections. Acute and convalescent sera from 4 monkeys were tested and a rise in titre of neutralizing antibody found in 1; the others had high titres in the acute phase specimen. 17% of 100 normal monkeys were found to have antibody. A monkey infected experimentally in the tongue showed a rise in antibody.

Ante-mortem examination of the anaesthetized monkey for ulcers is recommended for the exclusion of affected monkeys from vaccine production. In the central nervous system the restriction of lesions to the pons and medulla facilitates the differentiation from lesions due to poliomyelitis. *C. E. Gordon Smith*

IMMUNITY

MARKOV, W. & OBRETENOVA, K. Der dynamische Effekt beim immunisatorischen und infektiösen Prozess. [**Contrasted Immunizing Effect of Inoculation of Dead and Living Bacteria**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 151–9, 5 figs. [10 refs.]

The authors have set themselves to determine the respects in which immunity due to actual infection differs from immunity produced by inoculation with the same infective material which has been killed by heat. The infections produced were not lethal and followed a single injection, whereas repeated injections of the killed material were given. The organism used was *Salmonella abortus ovis*. The points of difference established were the following:—

The mild infection excited a greater production of agglutinating antibody than did the inoculation of dead material.

Inoculation of the killed bacteria produced an increase in polymorphonuclear leucocytes almost immediately whereas the mild infection was associated with a preliminary rise in the number and proportion of lymphocytes followed by an increase in polymorphs in the second week. There was also a late increase in eosinophil polymorphs in both types of infection. This appeared about the second or third month and was most marked in the case of animals treated with dead bacteria. It was also observed in both groups that the highest agglutinating titre corresponded with the period of fall in lymphocytes which, it is suggested, might be taken to mean participation of the lymphocytes in antibody production.

There was no evidence that a difference in bactericidal activity of the serum developed in the two groups or in their capacity for a non-specific phagocytic activity. (This was tested against *Staphylococcus albus*.)

J. W. McLeod

HOWARD, J. G., ROWLEY, D. & WARDLAW, A. C. **Investigations on the Mechanism of Stimulation of Non-Specific Immunity by Bacterial Lipopolysaccharides.** *Immunology*. Oxford. 1958, July, v. 1, No. 3, 181–203, 11 figs. [34 refs.]

After intravenous injection of ^{32}P-labelled lipopolysaccharide (prepared from a variety of bacteria) into mice or guineapigs a rapid accumulation could be demonstrated in the reticulo-endothelial system (RES). The rate of accumulation of ^{32}P-labelled lipopolysaccharide was slowed when an injection of non-radio-active lipopolysaccharide was given 30 minutes

previously, but if the interval between injections was increased to 48 hours the rate of clearance from the blood stream and consequent accumulation in the RES was considerably increased. This was accompanied by other manifestations of reticulo-endothelial activity.

Alternating depression and stimulation of the RES could be produced by the injection of Thorotrast with demonstrably increased resistance to *Escherichia coli* infection and decreased resistance to *Salmonella typhimurium* during the phase of increased RES activity. The RES could also be stimulated by injections of the lipid A component of bacterial lipopolysaccharide, but in this event resistance to both *E. coli* and *Salm. typhimurium* was enhanced.

The basis of non-specific immunity induced by bacterial lipopolysaccharide is discussed in relation to changes taking place in the properdin and reticulo-endothelial systems.

[This paper contains much detail, and interested readers are referred to the original.]

[See also this *Bulletin*, 1957, v. 32, 216.]

R. G. Sommerville

GREEN, D. M. **The Effects of Nitrogen Mustard (Methyl Bis (β Chloroethyl) Amine HCl) on the Immunological Response of the Rabbit. II. The Effects of Nitrogen Mustard on the Breakdown of a Bacterial Antigen in Splenic Tissue.** *Brit. J. Exper. Path.* 1958, June, v. 39, No. 3, 213–18. [12 refs.]

The appearance of antibody is delayed in animals which are given a course of nitrogen mustard and it has been suggested that this may be due to a delay in the breakdown of the antigen [this *Bulletin*, 1959, v. 34, 101].

Antibody production by the spleen cells of immunized rabbits transferred to normal rabbits is prevented if the cells are processed in any way, perhaps because the antigen has already been rapidly broken down to a non-antigenic stage.

To investigate this, rabbits were injected with a course of nitrogen mustard followed by a *Salmonella typhi* suspension 24 hours later. Their spleens were removed after an interval, processed (freezing, thawing and freeze-drying) and injected into normal rabbits.

It was found that the spleens of animals killed 24 and 48 hours after injection of the antigen did not initiate production of detectable agglutinins by recipient rabbits. But when these were injected with *Salm. typhi* 4 weeks afterwards there was a secondary type of antibody response which suggests that some antigen had persisted in the spleens of the nitrogen mustard rabbits.

A primary response was obtained if the spleens of nitrogen mustard rabbits killed at 72 and 96 hours, or normal untreated rabbits killed 24 hours after the antigen injection, were used. This is what would be expected if all the antigen had been broken down.

The retardation of antigen breakdown in the spleen of rabbits treated with nitrogen mustard was associated with a marked reduction in the number of polymorphonuclear leucocytes.

J. Nagington

SMITH, R. T. & BRIDGES, R. A., with the technical assistance of Enid THOMSON. **Immunological Unresponsiveness in Rabbits produced by Neonatal Injection of Defined Antigens.** *J. Exper. Med.* 1958, Aug. 1, v. 108, No. 2, 227–50, 2 figs. [56 refs.]

Rabbits given a single dose of antigen immediately after birth fail to show an antibody response. This paper describes experiments on the nature of this so-called immunological unresponsiveness. At least 4 or 5 rabbits, and sometimes considerably more, were used in each experiment and the antigen in most of the work was bovine serum albumin (BSA).

Rabbits given at birth 1 intraperitoneal injection of BSA, to which they did not form antibodies, were later given further injections of BSA and the responses to the secondary injections were determined. If less than 10 mgm. of BSA was injected at birth or if the primary injection was delayed beyond the first 2 weeks of life the rabbit showed a normal antibody response to later injections of BSA. Rabbits given repeated doses of BSA at intervals after the primary injection permanently failed to form antibodies to BSA. The period of unresponsiveness after a single injection at birth, if repeat doses were not given at intervals, was not permanent but lasted longer after a large primary dose than after a small one. In an unresponsive rabbit, injected antigen declined in the blood stream at a constant rate and did not show the phase of accelerated disappearance which follows administration of antigen to a normal rabbit. Injection of a suspension of lymph node tissue from an immunized normal rabbit led to the appearance of antibodies in the serum of the unresponsive animal.

The unresponsive state could be produced in rabbits with BSA, ovalbumin, human gamma globulin or human macroglobulin as the antigen but not with diphtheria toxoid, TAB vaccine, a streptococcal vaccine, tuberculin, BCG or a preparation of meningococcal endotoxin.

The authors suggest that the period of unresponsiveness lasts only as long as some antigen remains in the animal's body and that the residual antigen occupies an intracellular location.

I. B. R. Duncan

i. LANDY, M., SKARNES, R. C., ROSEN, F. S., TRAPANI, R. J. & SHEAR, M. J. **Inactivation of Biologically Active ("Endotoxic") Polysaccharides by Fresh Human Serum.** *Proc. Soc. Exper. Biol. & Med.* 1957, Dec., v. 96, No. 3, 744–7. [11 refs.]

ii. SKARNES, R. C.; ROSEN, F. S.; SHEAR, M. J.; LANDY, M. **Inactivation of Endotoxin by a Humoral Component. II. Interaction of Endotoxin with Serum and Plasma** [SKARNES, ROSEN, SHEAR & LANDY]. *J. Exper. Med.* 1958, Nov. 1, v. 108, No. 5, 685–99. [29 refs.] **III. Role of Divalent Cation and a Dialyzable Component** [ROSEN, SKARNES, LANDY & SHEAR]. *Ibid.*, 701–11.

i. "Insofar as they have been examined, all the endotoxin properties of polysaccharides, irrespective of

their source (*viz.*, bacterial, plant or mammalian), were annulled on incubation with fresh human serum but not with heated serum. Moreover, this action of fresh serum was independent of antibody, of complement, and of properdin."

ii. II. "A humoral substance which inactivates endotoxin *in vitro* has been shown to be clearly distinguishable from complement, properdin, and specific antibody. For the present, it is designated 'endotoxin-detoxifying component' or EDC.

"Animal species could be grouped in three categories with regard to the EDC activity of their sera; rat serum was highly potent; chimpanzee, dog, horse, and guinea pig sera were much less active; mouse, rabbit, and sheep sera exhibited no activity. The EDC potency of human sera varied widely ranging from high to barely discernible activity. In contrast to the variations of EDC potency in serum, citrated plasma from all species manifested high potency of about the same magnitude.

"The influence of time, temperature, pH, and concentration of reactants on the inactivation of endotoxin by EDC was examined. EDC activity in plasma and serum was found to be labile to heating at 56°C. for 1 hour. Bacterial endotoxins, derived by different isolation procedures from smooth and rough Gram-negative species, varied considerably in susceptibility to EDC action."

III. "The uniformly high potency of citrated plasma as compared with the limited capacity of serum to inactivate endotoxin *in vitro* was found to be a consequence of the anticoagulant employed in collecting the plasma.

"Addition of calcium to plasma suppressed the activity of its endotoxin detoxifying component (EDC) whereas the addition of calcium-binding anticoagulants rendered serum comparable to plasma.

"Dialysis of plasma resulted in a marked reduction of its EDC activity despite the concomitant elimination of calcium. EDC activity could then be fully restored upon the addition of calcium-binding anticoagulants.

"Resin-treated plasma, without added anticoagulant, had EDC activity equal to plasma obtained with calcium-binding anticoagulants. Following dialysis, resin-treated plasma also sustained a marked reduction in EDC activity which could be fully restored by calcium-binding anticoagulants. Restoration was also obtained with the dialysate even after ashing.

"These findings indicated that the suppression of EDC activity by calcium is not direct but is mediated through its effects on an anionic component of plasma which is required for inactivation of endotoxin by EDC."

GUSTAFSSON, B. E. & LAURELL, C. B. **Gamma Globulins in Germ-Free Rats.** *J. Exper. Med.* 1958, Aug. 1, v. 108, No. 2, 251–8, 2 figs. [16 refs.]

The serum proteins of 34 rats belonging to a colony bred under germ-free conditions were compared with those of 36 control rats living under normal conditions. The germ-free rats were aged between 50 and 150 days. Some control animals were given the identical autoclaved diet used to feed the germ-free rats, and the others received the same diet unsterilized. At the end of the experiment all the rats were bled to death. Serum samples were analysed by paper-strip and starch-gel electrophoresis.

The average gamma globulin concentration in the sera of the control rats was 0·49 gm. per 100 ml. and the average in the germ-free rats was 0·21 gm. per 100 ml. The authors consider that a more correct value for the germ-free animals would be 0·09 gm. per 100 ml., a figure obtained by subtracting a constant of 0·12. In electrophoresis of human sera they had previously found this adjustment necessary because the gamma fraction in an electrophoretic separation also contains other proteins than gamma globulin. The beta globulins were lower in the germ-free rats than in the control rats although the difference between the averages for the groups was less than with the gamma globulins. Other protein fractions were the same in both groups.

The authors conclude from these results that the normal bacterial flora of an animal must be the main stimulus to the formation of the serum gamma globulins. *I. B. R. Duncan*

BORSOS, T. & KENT, H. N. **Serum Gamma Globulin and *Trypanosoma cruzi* Agglutinin in Embryonic, "Normal" and Germ-Free Chickens.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 105–8, 1 fig.

"The progressive changes in gamma globulin content in the sera of developing embryos indicated here confirm earlier findings. Following absorption of the yolk by the newly hatched chick, the transmitted gamma globulin levels decline until the young birds attain immunological maturity. The mature birds show high gamma globulin levels as illustrated by the electrophoretic patterns. In contrast, germ-free chicks reveal low levels of gamma globulin which remain so even at 313 days of age; *T. cruzi* agglutinin follows the same pattern. These results strongly suggest that a close correlation exists between serum gamma globulin levels and the indicator antibody. They also suggest that chickens reared under germ-free conditions, after losing the maternal antibody, do not replace it with gamma globulin of their own to any significant degree. Further studies are needed in order to follow the serum protein changes in older adult germ-free chickens and their response to controlled antigenic stimuli."

VAN MARWYCK, C. Inkomplette Antikörper bei Infektionskrankheiten. [**Incomplete Antibodies in Infectious Diseases**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 116–23, 1 fig. [27 refs.]

The English summary appended to the paper is as follows:—

"Serological investigations with antigens of Salmonella, Pasteurella and Brucella using the agglutination, blocking and Coombs tests had the following results:

"1. Incomplete antibodies can be demonstrated frequently when complete antibodies are present.

"2. In specific diseases with low agglutinin titers incomplete antibodies may be found frequently showing even titers 1 to 5 steps higher.
"3. The problem, whether the production of incomplete antibodies is a precursor reaction cannot be answered on the basis of the clinical material available. The results of vaccinations point into this direction.
"4. Incomplete antibodies may give cross reactions with other types or groups of the same genus. Blocking and Coombs test seem to show rather genus than group or type specificity."

DELAUNAY, A., PELLETIER, Monique & HÉNON, Michelle. Mise en évidence d'opsonines bactériennes non spécifiques. [**Observations showing the Existence of Non Specific Bacterial Opsonins**] *Ann. Inst. Pasteur.* 1958, Aug., v. 95, No. 2, 211–14.

An aqueous solution of polypeptides prepared by any one of 4 different methods from calf thymus possessed the ability to provoke rapid agglutination of suspensions of 8 different bacteria when the polypeptide concentration varied between 0·1 and 0·4 mgm. per ml.

A culture of smooth *Salmonella typhi* was rapidly phagocytosed by guineapig polymorphonuclear leucocytes *in vitro* upon the addition of 1 mgm. per ml. of the thymic polypeptide. In the absence of polypeptide no phagocytosis was observed. *R. G. Sommerville*

RIGGS, J. L., SEIWALD, R. J., BURCKHALTER, J. H., DOWNS, C. M. & METCALF, T. G. **Isothiocyanate Compounds of Fluorescent Labeling Agents for Immune Serum.** *Amer. J. Path.* 1958, Nov.–Dec., v. 34, No. 6, 1081–97, 1 text fig. & 7 figs. (2 coloured) on 3 pls. [18 refs.]

"Two fluorescent isothiocyanate dyes have been synthesized for use in labeling antibodies. The advantages of these isothiocyanates over the corresponding isocyanates depend upon their stability in a solid form which allows their storage and use directly when needed. The substitution of a less toxic substance, thiophosgene, for the highly toxic phosgene gas offers added advantage.

"The dyes were successfully conjugated with antiserums against different antigens.

"Specific staining of the following antigens was carried out, using the direct and indirect techniques: *B. anthracis*, *P. tularensis*, *R. typhi*, and adenovirus RI-67."

ŚLOPEK, S., SKURSKI, A., MICHALSKA, E. & DABROWSKI, L. **Phagocytosis and the Antigenic Structure of Bacteria.** [Correspondence.] *Nature.* 1958, Nov. 1, v. 182, 1243–5.

The phagocytic reactions of *Salmonella*, *Shigella*, the Alkalescens-Dispar group, *Escherichia* and *Brucella* were studied by incubating a washed suspension of each strain with equal volumes of washed leucocytes and inactivated horse serum at 37°C. for 20 minutes. Films were made and the phagocytic index estimated by counting the number of bacteria ingested by 100 leucocytes and dividing by 100.

Surface antigens had a marked inhibitory effect on phagocytosis and the character of somatic antigens also influenced phagocytosis. Differentiation between S and R forms was possible because the presence of serum was not essential for phagocytosis of the latter. The authors suggest that this test is more delicate than serological reactions especially in the detection of transitional S-R forms. *Sheila McDonald*

ROWLEY, D. **Bactericidal Activity of Macrophages *in vitro* against *Escherichia coli*.** [Correspondence.] *Nature.* 1958, June, 21, v. 181, 1738–9, 2 figs.

Mouse macrophages from the peritoneal cavity were maintained *in vitro* in tissue culture medium without antibiotics. *E. coli* suspensions added to the macrophages were rapidly phagocytosed in the presence of heat-inactivated horse serum and more slowly in the absence of serum.

Viable counts of the preparations of phagocytosed bacteria showed an extremely rapid bactericidal activity by the phagocytes against those bacteria which had been treated with the inactivated horse serum. The horse serum alone was not bactericidal and the macrophages which ingested untreated bacteria were unable to prevent them from proliferating rapidly. Only when the bacteria had been exposed to serum could they be effectively killed intracellularly. *J. Nagington*

WAKSMAN, B. H. & MATOLTSY, Margit. **The Effect of Tuberculin on Peritoneal Exudate Cells of Sensitized Guinea Pigs in Surviving Cell Culture.** *J. Immunology.* 1958, Sept., v. 81, No. 3, 220–34, 9 figs. [22 refs.]

These experiments were made on washed peritoneal exudate cells from normal and tuberculin-sensitive guineapigs. The exudates were induced by the intraperitoneal injection of sodium caseinate or glycogen and the cells were maintained in surviving cell cultures in stationary tubes. The culture medium was 20% normal homologous serum in balanced saline to which varying concentrations of tuberculin or PPD were added. The cultures were studied by direct microscopy, total viable cell count, vital staining with neutral red and trypan blue, and by differential counts of stained smears. The exudates contained polymorphonuclear cells, lymphocytes and large macrophages, but the predominant cell was intermediate in size and appearance between a lymphocyte and a macrophage; this cell had considerable cytoplasmic basophilia and it ingested neutral red in a manner characteristic of macrophages.

The results of 20 experimens are described. The most definite findings were: (1) that the presence of tuberculous antigens produces at about 18 hours a definite fall in the number of cells present in the culture, followed 72–90 hours later by a relative rise as compared with the control culture; (2) that cells exposed to the antigen survive up to 90 hours longer than unexposed cells; and (3) that the change of the "intermediate mononuclears" into macrophages is hastened by the antigen.

In discussing the results, with regard to the nature of the usual delayed response to the antigen *in vivo* and to the relationship between delayed sensitivity and humoral antibody formation, the authors stress that as the observations were made in a fluid lacking factors necessary for the maintenance of exudate cells and in which circulating antibodies may have been present, any conclusions can only be tentative until they can be reproduced under more physiological conditions. They suggest that the "intermediate mononuclears" are comparable to the circulating monocyte and tissue histiocyte, and that the changing of these cells into macrophages is comparable to that which occurs *in vitro* from the stimulation by the tuberculin antigen. They also consider that the pleomorphism of the predominant cell in delayed reactions *in vivo* finds its counterpart in their *in vitro* reactions; the necrosis of classical delayed reactions was, however, not a major effect observed in their *in vitro* system.

Delayed sensitivity is generally accepted as being closely related to antibody formation, and if the authors' interpretation of their data is correct, in animals with delayed sensitivity 1 or more cells are so altered that under antigen stimulation they proliferate and change both morphologically and functionally to mature macrophages. Whether antibodies are released in this process is unknown, but perhaps all immunization processes produce cell alterations leading to formation of macrophages and antibody-producing plasma cells, and we speak of antibody formation or delayed sensitivity depending on which cell predominates. Delayed reactions undoubtedly frequently contain plasma cells and these may represent cells prepared for the antibody-forming reaction, responding to antigen at a local site instead of at a site of immunization. There is inconclusive evidence that shows that during immunization a stage of delayed sensitivity precedes the appearance of antibodies and if this is so, then there would appear to be among mesenchymal stem cells, reticulum cells, lymphocytes, monocytes and histiocytes 1 or more multipotent cells; such a radical idea can, however, only be confirmed by much further investigation.

S. R. M. Bushby

WAKSMAN, B. H. & MATOLTSY, Margit. **Quantitative Study of Local Passive Transfer of Tuberculin Sensitivity with Peritoneal Exudate Cells in the Guinea Pig.** *J. Immunology.* 1958, Sept., v. 81, No. 3, 235–41, 3 figs.

In these experiments donor cells were obtained from the cellular exudate produced in the peritoneum of tuberculin-sensitized guineapigs by the injection of sodium caseinate or heavy mineral oil, and in a few experiments they were from spleen homogenates. The cells were mixed with OT or with 50% glycerol, as a control, and injected either intradermally or intracorneally into unsensitized guineapigs. The reaction in the skin was noted after 24 hours by measuring the longest and shortest diameter of the area of induration and the thickness by means of a micrometer, measuring the thickness of a double fold of the skin, subtracting the thickness of the normal skin and dividing by 2. The volume of induration was calculated by multiplying this figure by the 2 diameters and by $\frac{3}{4}$ (an approximation of $\pi/4$) and this figure represents the main datum in the experiments.

The reactions were small as compared with the usual reaction of tuberculin in sensitized animals; they often contained 1–2 mm. of central necrosis and their appearances conformed to the description by METAXAS and METAXAS-BUEHLER [this *Bulletin*, 1956, v. 31, 388] of a passively transferred local reaction. High doses of tuberculin frequently produced smaller lesions than did smaller ones and this was attributed to the toxic effect of the tuberculin. Slightly larger reactions were produced with cells from the more highly sensitive animals, and in new-born or immature guineapigs no reactions were produced. The intracorneal injection produced opacities lasting 48–72 hours. In some experiments the cells and tuberculin were incubated together before being injected, in an attempt to demonstrate that the reactions were due to a substance liberated from the cells but, except for experiments in which the mixture was incubated for 20 hours, none produced a reaction. In the 4 experiments with spleen homogenates a slight reaction was produced in only 1.

In discussing these results the authors point out that the usual method of passively transferring delayed sensitivity is by injecting the cells intravenously and that the response is accounted for by either assuming that the cells release antibodies which render the host sensitive or that they themselves react with the antigen; the close relation shown between the size of these reactions with sensitized cells and the volume of cells injected supports, in the opinion of the authors, the latter contention; this is further supported by the intracorneal reactions.

The increase in volume at the reaction site is at least partly explained by assuming that the volume increase of the transferred cells, with or without actual cell multiplication, occurs as was observed to take place *in vitro* [see above]. The failure to produce reactions in new-born guineapigs may be due to the transferred cells failing to develop into macrophages through being in an unfavourable environment.

S. R. M. Bushby

Miscellaneous

GERSTNER, H. B. **Acute Clinical Effects of Penetrating Nuclear Radiation.** *J. Amer. Med. Ass.* 1958, Sept. 27, v. 168, No. 4, 381–8, 6 figs. [16 refs.]

This is an outstanding paper on the subject of damage to the population after atomic bomb explosions. The experiences of Nagasaki and Hiroshima are drawn on, and these are correlated with chemical information from reactor accidents, exposure to fall out etc. The author is able to predict some of the hospitalization needs of people overcome by a holocaust; there are 3 phases of acute clinical conditions which would call for organized direction by the medical personnel.

Effects of Penetrating Ionizing Radiation on Man
Schematic survey.

	Acute Radiation Syndrome, Form		
	Cerebral	Gastro-intestinal	Haemopoietic
Determining organ	Central nervous system	Small intestine	Bone marrow
Threshold dose, γ	2,000	500	100
Latent period	½–3 hours	3–5 days	3 weeks
Characteristic signs and symptoms	Lethargy, convulsions, ataxia	Diarrhoea, fever disturbance of electrolyte balance	Leukopenia, purpura, infection
Underlying Pathology	Inflammatory reactions in central nervous system, brain oedema	Denudation of gastro-intestinal mucosa	Atrophy of bone marrow
Time of death (if occurring)	Within 2 days	Within 2 weeks	Within 2 months
Cause of death	Respiratory arrest	Circulatory collapse	Haemorrhage generalized infection
Prognosis	Hopeless	Poor	Good
Source of information	Animal experiments	Animal experiments, bomb casualties, nuclear accidents	Bomb casualties, nuclear accidents, radiotherapy

One can do no better, to give the reader an idea of the scope of this paper, than reproduce the schematic survey on p. 383.

Here are 3 clear-cut conditions, all requiring essentially specific treatment. Each of these conditions is described in full detail by the author. The signs and symptoms are dependent on dose level and individual susceptibility. The haemopoietic form of the disease will probably pose the major problem facing any physician who finds himself amid these victims of catastrophic conditions.

[Few medical officers of health can afford to let this outstanding paper go unread.] *S. Russ*

MINISTRY OF HEALTH. NATIONAL HEALTH SERVICE. **Treatment of Anthrax, Botulism, Snake Bite and Rabies.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Sept., v. 17, 215–17.

This memorandum contains revised lists of centres in England and Wales which hold emergency supplies of sera for the treatment of anthrax, botulism and snake-bite (24-hour service); anthrax serum for prophylactic use; and rabies vaccine for active immunization and serum for immediate passive protection. The particular therapeutic and prophylactic agents held by each centre and the addresses and telephone numbers of the centres are given. *A. H. Phipps*

ASHER, R. **Why are Medical Journals so Dull?** *Brit. Med. J.* 1958, Aug. 23, 502–3.

The answer given is partly that their format is uninviting and partly that the articles they contain are too often poor presentations of interesting material.

"Style is what matters most; grammar, syntax, spelling, and punctuation are only useful conventions . . ." The important thing is to make reading easy by writing in a stimulating and lively manner. Authors who write ponderously "clog their meaning with muddy words and pompous prolixity; they spend little time in seeking the shortest, neatest, and plainest way of putting down their meaning". "Style is largely a matter of taking trouble, though many people wrongly regard it as a gift.

"Here is a sentence from a medical journal: 'Experiments are described which demonstrate that in normal individuals the lowest concentration in which sucrose can be detected by means of gustation differs from the lowest concentration in which sucrose (in the amount employed) has to be ingested in order to produce a demonstrable decrease in olfactory acuity and a noteworthy conversion of sensations interpreted as a satiety associated with ingestion of food.' All the author meant was: Experiments are described which show that normal people can taste sugar in water in quantities not strong enough to interfere with their sense of smell or take away their appetite."

Papers should in general be as short as possible. [This is all excellent advice, but the reviewer would also emphasize clarity and the importance of having something worth writing about.] *Charles Wilcocks*

Book Reviews

WORLD HEALTH ORGANIZATION. **World Directory of Medical Schools.** 314 pp., 1 folding map. 1957. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [25s.; $5.00; Sw. fr. 15.–.]

The most significant figures are perhaps the population per physician, indicating the present condition, and the population per new physician, indicating the relationship of output to the needs of the countries. The text of the Directory builds up to this summary. An original explanation with a summary of curricula gives such information as can be collected on medical education in the different countries of the world. There follows for each country, listed alphabetically, a written statement of variable but often considerable length dealing with the administration of medical education, the methods of school education, the conditions of admission to medical school with details of the curriculum, examinations, standards and methods of qualification or registration. There is a list of medical schools in the territory giving for each the ownership, the year of foundation, the numbers of teaching staff, of enrolled students, annual admissions, annual graduates, and the tuition fees. Not all of this material is of course strictly comparable from country to country, but an effort has been made to make a comparison of like with like. There is considerable interest in the individual statements and also in the summaries of information given in a series of annexes for the different continental areas, from which it is possible to amplify the outline information derived from the table which is reprinted below. All the countries of Africa except the Union of South Africa, Egypt and Algeria

ANNEX 8. WORLD TOTALS

Area	Population	Number of medical schools	Number of physicians	Annual number of medical graduates	Population per medical school	Population per physician	Annual number of medical graduates per 1,000 physicians	Population per new physician, *i.e.*, annual graduate
	Millions				Millions			Thousands
Africa	210·8	16	23,284	1,089	13·2	9,055	46·8	194
North and Central America ..	234·3	124	259,664	9,076	1·9	902	35·0	26
South America	121·0	53	48,263	5,308	2·3	2,507	110·0	23
Asia, Eastern ..	1,370·8	171	209,688	12,418	8·0	6,537	59·2	110
Asia, Western ..	82·5	15	16,951	868	5·6	4,869	51·0	95
Europe	619·7	253	665,522	37,222	2·4	931	55·8	17
Oceania ..	14·2	6	12,427	741	2·4	1,145	59·6	19
World total ..	2,653·4	638	1,235,799	66,722	4·2	2,147	54·0	40

have either more than 5,000 population per physician, or more than 100,000 population per new physician, or both, whereas in none of the countries of South America is this the case, though a few central American countries are still below this arbitrary standard chosen by the reviewer. In eastern Asia only Japan, Hong Kong, the Philippines and Taiwan meet such a standard while most of the countries fall considerably below it, some of their deficiencies being greater than those typical of Africa. In western Asia the situation is much more satisfactory and though few countries meet the standard, most approach it. Albania is the only country of Europe in which there appears by this form of measure to be remaining gross deficiency of medical practitioners, while in Oceania it is in New Guinea only that a similar defect exists. [This Directory should be on the bookshelf of all who are concerned with the standards and volume of medical education throughout the world, and also all who receive students from overseas countries.]

[For review of the first edition, see this *Bulletin*, 1953, v. 28, 998.] *G. Macdonald*

BORRIS, Wolfgang. Leitfaden der Hygiene-Praxis. [**Guides to Hygienic Practice**] pp. xvi + 262. 1958. [DM. 13.50] Leipzig C1: VEB Georg Thieme, Hainstrasse 17/19, Aufgang C.

This book is the fourth of a series on applied hygiene edited by Dr. Siegfried MÜNCHOW, director of the Hygiene Institute of Dresden. The first 3 books were on communal kitchens, foodstuffs and principles of bacteriology. The present book is, however, of different character in that it is primarily intended to be a handy reference book on present hygienic practice for use by health inspectors, welfare workers, municipal nurses, officials and others whose work concerns the care and health of the people. Its subject matter, which is set out in a long list of contents with many sub-sections, covers infectious diseases and their control; food hygiene; the hygienic control of the food industry in general, of dairies, of the sale of milk, of meat supply and of bakeries; the sampling of foods, environmental hygiene including water supply and sewage disposal. Much space is devoted to the relevant acts, regulations and memoranda. There is also a list of definitions of technical words and phrases.

The information given is remarkably extensive and is presented in very concise form. The book which is well produced should fulfil admirably the purpose for which it is intended. *M. E. Delafield*

UNITED KINGDOM: **History of the Second World War. The Royal Air Force Medical Services.** Vol. III. Campaigns [Edited by S. C. REXFORD-WELCH, M.A., M.R.C.S., L.R.C.P., R.A.F.] pp. xxv + 730, numerous illustrations. 1958. London: H.M. Stationery Office. [£5 5s.]

The third volume completes the medical history of the Royal Air Force Medical Services in World War II. It depicts the great odds which confronted the R.A.F. in the first 3 years of the war when Great Britain and the Commonwealth stood alone with small and inadequately equipped forces against a mighty, well equipped enemy, and had to spread, transport and maintain these forces for operations ranging from bases in the Arctic Circle throughout the coastal areas of Africa to the Cape of Good Hope in the south, and from the West Indies to the Far East. On the outbreak of war in 1939, the total strength of the R.A.F. was only 69,844 and that of the medical service was 2,421, of whom 268 were medical officers (148 regulars and 120 with short-service commissions). By 1945 the medical service had increased to a total strength of 23,250, of whom 2,671 were medical officers. With this 10-fold dilution of trained and seasoned personnel and the difficulties of transportation and of provision of equipment, it was not surprising that there were certain shortcomings, especially in remote areas such as West Africa and the Far East. Temporary personnel were given as much training as possible at home before being sent overseas, but naturally they had to become acclimatized to arctic and tropical conditions and had to learn many things the hard way, especially as there were not enough regulars to post to the innumerable small units (squadrons) which were a feature of the R.A.F. organization. This history records the fine achievements of the temporary members of the R.A.F. Medical Services and the great progress made particularly in preventive medicine in relation to food-borne and insect-borne diseases, which otherwise would have reduced enormously the efficiency and striking power of the R.A.F.

Though much of the information in this volume is primarily of value to those in the Services, there are large sections, particularly those on India and the Far East, Malta and West Africa, which are of considerable interest to civilians engaged in hygiene and preventive medicine in warm climates. In this connexion, West Africa was used as a proving ground (by the Army and R.A.F. in conjunction) to assess the value of various antimalaria measures in preparation for an all-out attack in the Far East, where the victory over malaria was the first step to final defeat of the enemy. Among the anti-measures tested were the efficiency of malaria suppressive drugs, screening of quarters against mosquitoes, newly introduced insecticides and various means of applying them to quarters as well as in aircraft, and of clearance and drainage schemes to reduce the mosquito population. In these matters, thanks to the action of the Resident Minister, the Army and R.A.F. worked in conjunction, so that there was no overlapping and labour was conserved. In 1942, Area Malaria Boards were formed in each Colony of West Africa, and they devoted their attention primarily to antimalaria work on airfields and R.A.F. camps, as the West African route became the pipe line to supply the Middle East. Medical officers, malariologists, engineers and the appropriate executives of the Public Works Services and the Armed Forces worked in close collaboration with most gratifying results. For example, whereas the incidence of malaria in the R.A.F. in West Africa was 840 per 1,000 per annum in 1940, it was reduced to 78 per 1,000 by 1944.

The chief diseases which affected the R.A.F. in tropical and sub-tropical areas were malaria, dysentery and gastro-enteritis. The incidence and severity of these

diseases were greatly reduced as a result of supplies of DDT, mepacrine and sulphonamide drugs becoming generally available from 1942 onwards. During the siege of Malta from 1940 to 1943, sandfly fever was the main cause of sickness among R.A.F. personnel, and, on an average, led to 14 days' non-effectiveness in each case, and was a serious handicap to the striking power. This state of affairs was largely due to the widespread heaps of rubble from bombed buildings which provided ideal breeding grounds for sandflies. In 1945, however, DDT became available to treat the rubble and quarters, and the incidence of sandfly fever was materially reduced. It was of interest to note that a somewhat similar high incidence of this disease was prevalent among the R.A.F. and other Services in the years before 1922 (the incidence being about 120 per 1,000 per annum) when the R.A.F. Sandfly Commission investigated the matter. This incidence was reduced 10-fold within 2 years as a result of the Commission's recommendations—the removal of rubble and the levelling of broken ground and its regular tarring; the control of vegetation near habitations; pointing and filling-in of cracks in walls; provision of electric fans; and sandfly proofing of buildings.

The editor of this volume is to be congratulated on such a concise, readable and well-illustrated record of the activities of the R.A.F. Medical Branch in the field under strenuous conditions of climate and air warfare.

[For Parts I and II, see this *Bulletin*, 1955, v. 30, 1034; 1956, v. 31, 688.] *H. E. Whittingham*

Notices

AIR POLLUTION CONTROL ASSOCIATION

4400 Fifth Avenue,

Pittsburgh 13. Pa.

The next annual meeting of the Air Pollution Control Association will be held June 22–26, 1959, at the Hotel Statler in Los Angeles, California. This meeting will include technical sessions and exhibits. Details may be obtained from the Executive Secretary of the Association.

UNIVERSITY OF DURHAM
KING'S COLLEGE

DEPARTMENT OF CIVIL ENGINEERING
PUBLIC HEALTH ENGINEERING SECTION

Symposium on the Treatment of Waste Waters
14–19 September, 1959

(The programme and application form to attend the Symposium are obtainable from the Department of Civil Engineering.)

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